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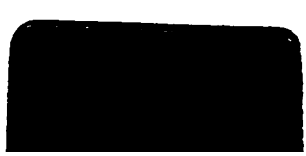

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OF

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BY

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EDITED BY

THOMAS L. STEDMAN, M.D.

NEW YORK CITY

IN TWENTY VOLUMES

VOLUME XIV

INFECTIOUS DISEASES

NEW YORK

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SCARLET FEVER.

BY

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VOL. XIV.—1

SCARLET FEVER.

History.

THE first clinical description in connection with the name scarlatina or scarlet fever comes from Sydenham (born 1624, died 1689). The first complete edition of his works was published in 1685 in London, and his observations on the fevers were made at least fifteen years before this. Subsequent editions are quoted by authors who have written on the history of scarlet fever (for instance, Hirsch, the Geneva edition of 1736), and the historical perspective has been very much interfered with in this manner. So far as the name of the disease is concerned, Häser makes the statement that Corradi claims that the term "mala da scarlatina" was first used by Lancelotti in 1527; Häser and Johannessen are by way of giving absolute credence to this statement; as the latter says, "the name does not come from England, as Bohn thinks, nor from Sydenham to whom it is referred by Hirsch." In regard to the claim of the Italians, Hirsch puts it very aptly when he says that although Lancelotti may have used the term scarlatina, it is doubtful whether scarlet fever was meant by it. And Johannessen finally comes to the conclusion that Sydenham and Morton were the first to have introduced scarlatina to the general medical conscience. He might have added more aptly that the medical concept of scarlatina comes from Sydenham.

It is difficult to state positively where the first clinical description is found. The reasons for this are many. Most, for instance, states that garrotillo, which first appeared in Europe about 1610, and scarlatina are the same. For him, then, all descriptions of garrotillo, which probably was diphtheria, have reference to scarlatina, although the exanthem and desquamation are rarely mentioned in the excerpts he gives from his authors. Then there is that indefinite term miliaria, curiously enough still insisted upon as a pathological entity by Hirsch, which gave rise to much confusion in historical research. Lastly, many authors knew only morbilli, measles; any form of eruption (macular, papular, or pustular) was called morbilli. Even Morton (1698) looked upon scarlatina as the same as measles (*vide* the often quoted "Hunc morbum prorsus eundem esse cum morbillis

censeo"), although his chapter is headed de morbillis et febre scarlatina. A curious explanation for this statement is offered by Gütschow (see Most), who claims that jealousy prompted Morton to persist in calling scarlet fever measles. Confusion in terminology and diagnosis as between measles and scarlatina did not cease until the beginning of the eighteenth century. Principally for these reasons and, in addition, because the very old medical writers used medical terms like aphthæ, ulcera, and many others quite indiscriminately, a diagnosis of skin lesions has almost become impossible from their descriptions. It seems, therefore, futile to go back into antiquity for the first accounts of this disease, although this has been repeatedly done and is being done by excellent authors. Even Johannessen cannot resist the temptation of speculating upon this subject, and mentions El Wagidis, the Justinian pest (believed by Krause to be scarlet fever), Malfatti's view of the Thucydidean pest, the description of some of the older Frenchmen, and finally Rhazes' "de variolis et morbillis."

The first description of an epidemic that could be called scarlatina is found in Ingrassias of Palermo (1560). This is followed by the description of another at Poitiers by Jean Coythar (1678, *vide* Barthez et Sanné); then of one at Giessen by Gregorius Horst (1624), and finally a clear, unmistakable clinical description by Danniel Sennert and his son-in-law Doering, the former in Wittemberg and the latter in Breslau (the dates variously given, 1627, 1654, 1676). Then appeared Sydenham and Morton, the former with a description of very mild epidemics, the latter with that of a severe form. With these two authors, especially the former, the disease receives its nosological position.

The position as to the historical importance of Sydenham, it seems to us, is the following: while the symptoms had been described by Ingrassias, Coythar, Horst, Sennert, and Doering, it remained for Sydenham to combine a description of the disease with a positive name; in this way giving it an independent position, and even more than that giving it an entity, causing us to be conscious of its existence.

From the time of Sydenham and Morton until the beginning of the eighteenth century little is heard of the disease. Huxham and Fothergill described epidemics occurring in Great Britain in the years 1739, 1742, 1744, 1746, 1747, 1748, 1751, 1752, 1753, the epidemics varying in intensity. In France there was quite an epidemic in 1750; the whole of Europe was affected by a mild epidemic in 1790–95, and by a very severe one in 1795–1805 (forty thousand children, it is said, dying in Saxony alone). It is difficult to state when it appeared at a given place for the reasons given above. Thus, ac-

counts come from Scotland as far back as 1661 (Sibbald *vide* Hirsch), 1716 in Berlin, 1717 in Florence, 1740 in Denmark. It is impossible to say when it first appeared in Asia and Africa. It was first observed in 1735 in North America (in the New England States), in 1829–31 in South America, in 1847–48 in Australia.

Geographical Distribution.

Scarlet fever occurs most commonly in Germany, France, the Netherlands, England, Scandinavia, Prussia, the United States of America, and Canada. It is found in the North (Iceland) as well as in the South (Italy, Turkey, Greece). It is rare in Asia and Africa, especially in Egypt, Abyssinia, Tunis, Senegambia. Exceptions to this rule in Asia are found on the coast of Asia Minor, where the disease is very malignant. In Syria, Mesopotamia, Persia, and Arabia the disease occurs only sporadically; in India only imported cases are observed and, it is said, the disease never occurs in epidemic form. Many of the observers unite in the statement that when a case is reported occurring away from the coast or from direct European contact, errors of diagnosis have been made. In China the disease does occur, but very rarely, and in Japan it is unknown.

In Australia the disease seems to have developed as it does in all civilized countries, sometimes mildly, at other times with greater severity.

In America the disease is found in all parts as far north as Greenland and as far south as Peru. Within this limit there are portions that are more or less free from the disease. In the United States scarlatina is rare in the Southern States; indeed, it is very common to find the inhabitants of the Southern States very much more alarmed over a single case of scarlatina than over an epidemic of yellow fever. In Southern California epidemics are practically unknown, while in the northern part they have occurred repeatedly. Upon the whole, with these exceptions, the disease occurs at all times of the year in the United States and never seems to die out. The disease is not common in Central America, but epidemics of a malignant type have occurred there repeatedly. Numerous epidemics have been observed in the West Indies. In South America scarlatina is found in about the same frequency as in North America, and all parts seem to have suffered.

Etiology.

We are justified in the assertion that the poison of scarlet fever is a contagium vivum. But this statement must be accepted as expressing a scientific belief, not actual knowledge. Of the infectious dis-

eases, the acute exanthemata are among the few whose cause has not been isolated. And yet, if we may judge from what we know of the cause of the other infectious diseases, there remains only the assumption of a contagium vivum as the cause of the eruptive fevers.

Since the days of Sydenham the medical profession has been engaged in studying the properties of the scarlatinal poison, and while some of these have been accepted by the majority of observers, many are still under discussion, a fact that need cause no surprise when we are asked to judge of the nature of a body without being able to isolate it. If we were able to know all the properties of this body, such knowledge would be sufficient even without its isolation; but if, disregarding this physical improbability, we take into consideration that this knowledge would be the result of centuries of observation by hundreds of observers, it would be readily admitted that absolute knowledge is out of the question. So that here, as elsewhere, we must be guided by the gathered experience of the past, and the observations of the present at the same time, making due allowance for the widely differing opinions which we shall have constant occasion of taking into consideration.

If we grant that the poison of scarlatina is a contagium vivum and admit the truth of *omne vivum ex ovo*, the only logical deduction we can make is that each case of scarlatina has been produced by some preceding case. We must be permitted to leave out of consideration the discussion of the spontaneous origin of scarlatina, although excellent observers have been found to uphold this view. Either our view of the nature of the poison is correct and there can be no spontaneous generation, or this is not correct and we are not justified in drawing any conclusions whatever. Cases of spontaneous origin of scarlatina are like the evidences brought forward twenty-five years ago in favor of *generatio æquivoca;* there is always a leak of some sort in the apparatus, there will always be found some trifle that has not been taken into consideration.

Bacteriology.

The investigations into the exact nature of the poison were first begun by Hallier (1869). In order to find the poison, the blood, the urine, the scales of desquamation, the glands, and the sweat were examined. At first examinations were made only in the most rudimentary way with lenses of comparatively low magnifying powers; then with these and inoculations upon the lower animals, and finally with all the precautions laid down by R. Koch. Hallier found a micrococcus within the corpuscles of the blood or adhering to them,

which he called tilletia scarlatina. Hofman (1870) found a micrococcus in the sweat. Coze and Feltz (1872) found bacteria 6 μ long in the blood. They inoculated rabbits with this blood, producing death. The blood of these rabbits inoculated upon others, was followed by the same result. Riess (1872) found what he supposed were lower forms of life in the blood (punctate forms), but both cultures and inoculations were negative. Klebs (1875) described his monas scarlatinosum, which he found in an inguinal gland of a patient with scarlatina. This consists of a sphere made up of micrococci which develop into bacteria. Tschamer (1879) presented a most original view. He found micrococci and bacteria in the blood corpuscles, scales of desquamation, and in the urine. He also found some spores, and a cryptogam which he calls verticillium candelabrum (found in nature upon rotten wood); this, he claims, is a stage of development from the micrococcus. He inoculated himself, produced a superficial inflammation, found cocci in his blood, and came to the conclusion that he had produced scarlet fever in himself, proving this by the presence of these cocci in his blood. Eklund (1882) found cellular bodies in the urine, which he called plax scindens, also found by our countryman Octerlony, who has found this organism in the blood as well as in the urine. Eklund found this organism in "the soil, in water, on mouldy walls, and on mouldy paper." He found innumerable masses of this parasite on making microscopical examinations of the soil and water of muddy places, and of excavations dug for the purpose of laying water-pipes. Scarlatina immediately broke out among the children of a family living close to the place where the earth had been dug up in order to lay water-pipes, and who could not help breathing the exhalations from the water evaporating from these excavations during the summer days. No inoculation experiments were made by Eklund, "because he considered it contrary to his duty as a physician to expose even animals to mortal affections." Roth (1883) produced an ulcerative inflammation of the eyelids in the hen by inoculation of scales. Pohl-Pinkus as well as Klamman (1883) described micrococci upon the inner surface of the scales of desquamation and also as occurring in the mouth. The former is the first one to insist upon disinfection of the mouth. Finkelnburg (1887) has also isolated micrococci, but with little result.

We now come to the consideration of a discussion that promised much etiological outcome. Edington (1887), after having with Jamieson thoroughly sterilized the skin, found in the scales of scarlet fever patients, as well as in their blood, a great many lower forms of life: sarcina lutea, streptococcus rubiginosus, micrococcus capsiformis, bacillus arborescens, ascobacillus, bacillus fulvus, the diplococcus

scarlatinæ, and lastly the bacillus scarlatinæ which is pathogenic. He describes its biological properties as follows: It forms rods 0.4 μ thick and 1.3–1.4 μ long, which are usually united in long threads; cultivated upon bouillon or milk after a short time a tough membrane is formed. The bacillus has motion. Gelatin is rapidly fluidified, but here also a membrane is formed. The bacillus was found in cultures from the blood with great regularity after the third day, and after three weeks in the scales of desquamation. Rabbits inoculated had a temperature of 39.4°-41.1° C. and erythema followed by desquamation, and the bacillus was found in their blood. In guinea-pigs the same results occurred, except that the erythema was more marked. A calf inoculated with the bacillus died after twelve hours with severe changes in the liver, kidneys, heart, and pleura, with violent congestion of the pharynx and mucous membrane of the tongue. Another calf had a temperature of 40° C., all the symptoms of scarlatina, including rash and desquamation on the sixth day.

Unfortunately, soon after this publication W. R. Smith showed that this same bacillus could be obtained from the scales in dermatitis, and that in all probability the bacillus scarlatinæ was the ordinary bacillus of sepsis. Duclaux also showed that the antiseptic precautions taken by Jamieson and Edington, in order to secure scales free from contamination of air bacilli, were insufficient. Finally, a committee was appointed by the Medico-Chirurgical Society of Edinburgh which reported as follows upon the views of Edington: Out of ten cases of scarlatina the bacillus was found three times; of nine cases cultures from blood were followed by results in four, and cultivations from the scales as well as inoculations in animals were negative.

Before this time (1885) Klein had published most interesting observations, which were followed up by long discussions on the relation, supposed to be that of effect to cause, of scarlatina to a certain disease in cows observed by him at Hendon. His attention was first directed to the subject by an epidemic of scarlatina in London, in a quarter where the milk supply came from Hendon, in which place the cows upon one farm were affected by a peculiar disease, which Klein considered scarlatina. This disease affected fresh cows especially, and was transmitted mediately and immediately from one cow to another. Two or three days after the beginning of fever the eyes began to swell, on the fourth to the sixth day there appeared an eruption around them, and desquamation took place about the third or fourth week, accompanied by loss of hair. With the eruption there was a purulent discharge from the eyes and nose. A dry cough and rapidity of breathing were present during the first fourteen days of

the disease. Pharyngitis and swelling of the submaxillary glands and diarrhœa occurred in severe cases. Five to six days after the beginning of the disease one or more teats began to swell, and then there appeared two to four vesicles of the size of a pea or bean, without the previous development of a papule, which were destroyed by milking and left a crust which took from five to six weeks to fall off. On the hind quarters and external aspect of the posterior extremities there appeared an eruption leading to the formation of crusts and falling out of hair, but leaving no scars. Inoculation with the secretion from the ulcers produced similar ulcers upon the teats of the cows inoculated. In dogs inoculation was very successful; not so in guinea-pigs. Post-mortem examination revealed pleuritis, circumscribed pneumonic spots, hepatitis, and glomerulonephritis. In the ulcers diplococci, sometimes arranged as streptococci, were found. These stained with fuchsin, gentian violet, and methyl blue; they did not fluidify gelatin but formed white colonies. As the result of his experiments and investigations, Klein does not hesitate to consider this lower form of life as the cause of scarlatina, and the disease of the cows at Hendon as bovine scarlatina.

After this publication there followed quite a number of articles. Thus it was shown by C. B. Brown that the peculiar disease described by Klein was not confined to this one farm at Hendon, but that it occurred at various other dairies from which scarlet fever was not spread by the milk. Thin stated that the milkers at Hendon considered themselves and the cows as suffering from cowpox, and Crookshank, who observed the same epidemic among cows at Wiltshire, stated that it was cowpox, and that of three hundred consumers of the milk from these cows not one had scarlatina; and Thin as well as himself came to the conclusion that the streptococcus scarlatina of Klein was nothing more nor less than the ordinary streptococcus pyogenes; so that every point claimed by Klein seemed to be disavowed by other observers. Sifting all the evidence, Klein finally says that however one may think about the nature of the streptococcus, he is still prepared to state positively that scarlatina arises from the same disease in the cow.

Lastly, Mme. M. Raskin presented to the Congress at St. Petersburg (1889) the results of her investigations. Among a great many lower forms of life she found a peculiar micrococcus at the onset of the disease, in the corpuscles of the blood. After death it was found in the viscera, in the mouth, and on the skin. It was pathogenic in rabbits and guinea-pigs, but did not produce true scarlatina.

From all that has been said it will be seen that the microbe of scarlatina has not yet been discovered. It would be futile to try to

find the reason for this fact; we simply wish to verify it. In looking through the literature just reviewed, one is struck with the observation that many investigators have found a large number of lower forms of life, but these in the majority of instances were micrococci. Again, if we look at the reports of the bacteriology of the disease, together with the pathogenic manifestations of these lower forms of life, it will be seen that the streptococcus is the one schizomycete which is principally found. Before the days of Koch's methods, micrococci and streptococci were practically identical (Billroth, 1874, who introduced the term, believes that some micrococci arise from streptococci), so, that, undoubtedly, many other observers did see the streptococcus. The question that arises is: Are we dealing with a peculiar kind of streptococcus, one which could cause scarlatina? Babes, although finding some differences between it and that of Rosenbusch, does not hesitate to declare their identity. Fiessinger d'Ordronnaux (1893) and Berger (1896) believe that the streptococcus is the cause of scarlatina, while D'Espine and Marignac (1895) claim to have found a streptococcus in the blood and upon the tonsils which differs materially from that of Rosenbusch. None of these investigations have been verified, but they simply go to show the importance of the streptococcus in scarlatina. If to this there be added the further knowledge that has come to us concerning the manifestations of pus-producers, it will not be strange if finally a specific streptococcus may be found.

Having verified the fact that the bacteriologists have not as yet been able to find the contagium vivum of scarlatina, it becomes our duty to investigate the properties of this virus from the point of view of the clinician. It will be astonishing to find what differences of opinion exist even in regard to the subjects that can be considered as elementary. But this is not strange if we take into consideration the fact that clinical observations cannot be reduced to the simplicity of test-tube observations. When the time arrives in which the bacteriologist and the chemist give us even greater assistance than they do today, these contradictions, usually the result of some slight error in one of the terms of the equation, will disappear. For the present, therefore, we must be permitted to draw our conclusions from the accumulated experience of several generations of physicians, always being mindful that until the contagium of scarlet fever is actually isolated, these conclusions must be tentative.

Mode of Origin

The finding of one patient with scarlatina always permits the conclusion that he has become infected with the disease by another patient. Strong objections have been offered to this proposition. We have, here as elsewhere, the theory of the spontaneous origin of disease, *i.e.*, the spontaneous origin of the cause anywhere in nature. This doctrine must persist or go under with the whole subject of spontaneous generation. If any can be found who believe in *generatio æquivoca* elsewhere, there is no reason why they should not believe in the spontaneous generation of infectious diseases.

A second method of propagation is supposed to be scarlatina in man which may have had its inception in scarlatina of non-human origin. To this class belong all those cases in which it has seemed impossible to trace a connection between them and previous ones. As was referred to before, Tschamer, Roth, and Klein claim to have found an origin outside of man, and it will be seen that there is here a ready explanation of cases in which the origin was formerly considered as being spontaneous. Unfortunately, the evidences of the animal origin of scarlatina are far from conclusive, and it is more than probable that C. B. Brown's statement as to the infectiousness of milk is true, that the infection of milk must have been due to the cases of scarlatina living in the immediate neighborhood of the farms from which this milk came. Also it is true for animals as producers of scarlatina. The animals are only the media which carry contagion from one human being to another. When sufficient care is exercised in examining all the surroundings and handlers of the milk supply, there will always be found a case of scarlatina which has contaminated the milk. That outbreaks of scarlatina are due to contamination of the milk cannot be doubted. An epidemic at Plainfield, N. J., was found to be due to this cause, but the infection came from one of the employees, who, having a mild case of scarlatina, continued to assist in handling the milk.

Finally, it is necessary to take into consideration the miasmatic origin of scarlatina as an exception to the truth of the proposition of the human origin of the disease. This was supposed to be due to the *constitutio aeris et terræ et constitutio annua*, and explained both the origin *de novo* of scarlatina outside of man and also the internal human arrangement of morbific causes which resulted in the production of scarlatina spontaneously. Wendt (1819), in the florid style of this period, states that "the most common cause of the so-called new diseases (diseases arising without having historical rec-

ords) is found in the *constitutio aeris et terræ*, in that mysterious management of nature by means of which are produced those changes in the air and the earth which surround us as with a vise of iron and which occupy the foremost place in producing and predisposing causes for all our diseases. That scarlatina is propagated by contagion no one can doubt, but it is just as true that not every case has arisen from contagion, and that under favor of the *constitutio annua* it may develop from the living conditions of the individual. Whence came this disease when it appeared for the first time? Verily not from contagion! There is hardly one of the infectious diseases which under given circumstances cannot develop without contagion." Propositions like these are hard to disprove, but, fortunately, it is harder to prove them. If we state that these doctrines were propagated all over the scientific world as late as twenty years ago (Richardson, Barthez and Rilliet, Guersant, and many German authors) it will be seen to what desperate straits etiological investigators were pushed. It was only, however, after the days of bacteriological investigation set in, beginning with Klebs and v. Recklinghausen and developed completely by R. Koch, that the majority of observers was contented to give up the spontaneous origin of scarlatina altogether, and was willing to believe that one case of scarlatina always presupposed the previous existence of another case. This being the case, it follows that scarlatina can be contagious only in two ways: first, immediately; secondly, mediately.

Immediate contagion is meant to express that form of contagion when the healthy person contracts the disease by direct contact with the scarlatinal patient. There has arisen in Germany a school of hygienists headed by v. Kerschensteiner of Munich, which claims that "variola, scarlatina, and measles cannot be transmitted by means of a third person who is healthy," the first thesis of whose belief is "that the most common form of transmission in these diseases is the direct, coming from the patient." No one doubts that these methods of transmission do exist, but there is abundance of absolute proof as to the error of the first proposition, as will be shown farther on, and there is sufficient reason to argue concerning the accuracy of the second proposition. In the present state of our knowledge it is given to no one to make such a statement with such dogmatic positiveness, although the chances are largely in favor of its being true. When we see the reports of large epidemics being started by the ingestion of infected milk or by the handling of infected belongings, it certainly requires some temerity to say in what number of cases the origin of scarlatina was mediate or immediate. That direct contagion occurs in a large number of cases (how large no one knows),

cannot be doubted. Much doubt exists, however, as to when and how this contagion takes place. The first question presenting itself is where the poison is localized in the patient. It stands to reason that the first places it would be sought for would be those in which would be found anatomical manifestations, and such, as a matter of fact, has been the case. At first it was principally the skin that was held accountable for the spread of scarlatina. Latterly the skin is being disregarded as a source of infection, and much is made of the throat. Dowson (1893) tried to establish the fact that the first and essential lesion of scarlatina was to be found in the throat, just as a chancre is the primary and essential lesion of syphilis. This has been taken up especially by the French authors, and immediate contagion has been explained through contact with the secretions from the throats of infected patients. While as yet they are unwilling to admit the non-infectiousness of the desquamating skin, they are disposed to think this is caused by contact of the secretions of the throat with the skin. The observations of Lemoine, to be quoted hereafter, are responsible for this status of opinion. As to the time of contagion, the views again can be best shown by quotations from v. Kerschensteiner and other authors. The former says "the most favorable conditions for contagion exist during the stage of eruption and acme of the exanthem, the most unfavorable during desquamation." Girard claims that contagion occurs only during the first few days. Lemoine, Sevestre, Vogl, Mabboux, and a great number of English authors (Barclay, Longhurst, Cammeroom, Bandsom, William Squire, Parkes, Whitte) claim that the contagion exists during the stage of eruption, even during the period of invasion. Comparisons have been drawn between the contagiousness of measles and that of scarlatina during the preëruptive period. This must of necessity be fallacious, as it must be remembered that the enanthem of measles appears from one to four days before the exanthem, while in scarlatina it rarely develops longer than twenty-four hours before the eruption appears. The enanthem really must be looked upon as an eruption, as it shows the primary local effect has been followed by the general constitutional manifestations. It is not, therefore, astonishing that measles is contagious from one to four days before the eruption appears, but it would be quite extraordinary if this were the case in scarlatina. If the contagion does exist during the preëruptive period, it must be very slightly developed. In a large experience with scarlet fever, the author has never seen a second case arise from exposure to the patient during the preëruptive stage. Indeed, it is his experience that the disease is not very contagious even during the first day of the eruption.

That contagiousness does continue during the period of desquamation can be shown by any number of observations. The case of Sanné, which is so often referred to in French literature, is as follows: A man had a severe attack of scarlatina at Sédan, beginning on the eighth of January, 1865; he was isolated for six weeks, but transmitted the disease to a relative, who was in the habit of visiting him. When he was allowed to go out he went to the country, where he remained one month and then went to Paris, arriving on the 22d of March. On the same day he visited some friends, in whose house there was a boy, whom he caressed and held on his knee. Eight days afterwards the boy was taken with scarlatina, *i.e.*, seventy-three days after the appearance of the first scarlatina.

Naturally other explanations besides those of transmission by the scales have been offered for this case, but so excellent an observer as Sanné can be trusted as having eliminated all sources of error before he was willing to report this as a test case and before he came to the conclusion that the period of desquamation is the most dangerous for the transmission of the disease. The cases of Spear and H. C. Wood and of Cammeroom seem to bear evidence in the same direction. Johannessen, in an epidemic at Lomeethal, was able to study the conditions of transmission very carefully. In twenty-five families the patient who caused the disease in six instances was in the first week, from the second to the sixth week in seventeen instances, and twice later (indirectly by means of bedding), so that in the great majority of instances infection took place during the period of desquamation. Ashby keeps his patients in the hospital for forty-two days. He does not discharge them until desquamation has ceased, and yet he claims that two to four per cent. of his patients are infective, as is shown by return cases. It would be idle to multiply references, as most living authorities are agreed upon the possibility of infection during the period of desquamation. Lemoine, and curiously enough Vogl and v. Kerschensteiner, made their observations upon soldiers, and while the former does not absolutely deny the infectiousness of the scales, he claims that the primary infection of scarlatina is found in the throat and only on such things as come in contact with its secretions. He cites, in favor of this view, several instances in which soldiers came to the lazareth or went to their families without transmitting the disease, and also the case of his own child, which was infected by himself as a result of not having taken precautions in cleaning his face after a patient had coughed saliva upon it. Vogl's observations seem to show that scarlatina is not infectious during the period of eruption and desquamation; but, as his observations were made only upon soldiers and their male

nurses, one cannot refrain from thinking that the results might have differed if he had had to deal with children, that is, subjects not protected by previous attacks. So much the more is this the case in that he is willing to admit that in some instances the mode of transmission could not be detected. In order to be perfectly safe, it is necessary to admit then that the contagion exists in scarlatina from the inception of the disease until desquamation has been completed, that is for about six weeks. The existence of cases of scarlatina sine eruptione certainly emphasizes the fact that the poison may in a certain number of cases limit its activity to the throat; but this by no means precludes the view that it may also be found upon the skin, especially as its manifestations are found there in the majority of instances.

In order that scarlatina can be transmitted immediately, the contact must be quite close, such as touching, kissing, inhaling the breath, direct contact of the mucous membrane of the throat with the virus. The author has seen numerous instances in which children have been brought in close proximity with scarlatinal patients without touching them and have in all instances escaped infection. One instance especially deserves mention. In one of two adjacent city houses scarlatina broke out. The children affected with scarlatina were in the habit of playing with the children in the other house. As the cases were mild ones, the children could not be kept in bed and came to the windows in the rear of the house. These windows were not more than nine feet from the windows of the house in which the non-infected children lived. The distance was too great for the children to touch each other, and while nothing passed from house to house, the sick and well children were constantly conversing with each other, and still not one of the non-infected children became infected. This seems to prove that the scarlatinal poison cannot be carried by currents of air. Lemoine, Cadet de Cassicourt, and Sylvester seem to have had similar experiences.

The mediate transmission of scarlet fever takes place by means of either animate or inanimate things. If we can show that mediate transmission takes place at all, it goes without saying that this proposition is correct, for it is absolutely indifferent whether the medium be animate or inanimate. If it be animate, it may still be the vehicle for transmission, unless we accept with v. Kerschensteiner that in case of its being a human being, it is necessary that it have scarlet fever. But this latter proposition cannot be taken seriously, as any one with a large experience can prove. The case quoted above from Lemoine is in direct evidence. The author has had occasion to study the matter carefully and has never found it a postulate that the human carrier of infection must be ill in order to carry the virus.

He has for many years been connected with a hospital in which the means for isolation were not up to the modern standards. In this hospital there has been built an annex in which contagious cases can be treated, but at the same time it has been necessary to treat the overflow in some of the large wards. Most of the contagious diseases, notably the exanthemata and diphtheria, are confined to children. Therefore the interne of the children's service treated both the healthy children and those affected with contagious diseases. The nurses, however, were kept absolutely separate. The annex and the wards are in the second story, the children's ward upon the ground floor and some distance removed (from six hundred to one thousand feet). It must be added that the infected children are never admitted to the children's ward, but immediately sent to the places where they are to be treated. For scarlatina this can be carried out, as children are rarely brought to the hospital in the period of invasion. It has not infrequently happened that scarlet fever has been brought to children in the children's ward by the interne, as it could not be brought by the nurses, and was brought to children who had been in the ward for a sufficient length of time, so that infection before entrance was out of the question. In no instance has the interne complained to the chef of being ill, and in one instance two separate infections took place at such difference of time that it was impossible for the same interne, if he had been ill, to remain infectious.

Transmission by physicians is recorded frequently enough and not infrequently to their own children. Osler, Loeb, Lemoine, v. Ranke, Wolfsteiner, Hirsch, Wertheimer, Rezek, have all reported clases in which the physician has been the unfortunate medium of transmission. In Loeb's case his own child was infected by another physician, who had been to see a case of scarlatina in another city. The child had sat upon the doctor's lap and played with him for some time. In Worms, where Loeb lived, there was no scarlatina at the time. This seems a case from which conclusions can be drawn without danger of error.

That inanimate objects can be media is admitted on all hands. Food, bedding, letters, clothing, indeed anything that has been in contact with the scarlatinous patient may carry the contagion. The virus remains active for a great length of time. W. Boeck reports a case in which two children of a physician acquired scarlatina by playing with locks of hair that had been cut from the heads of two children dead with scarlatina, that had been enclosed within a drawer for twenty years. Johannessen mentions several instances in which the poison must have retained its virulence from two to four years. While no other cases are recorded in which the virus has retained its activity

for so long a time, many are on record in which it was still active for many months, and v. Hildebrandt's coat transmitted the disease, although it had not been in contact with scarlatina for eighteen months.

Inoculations.—There is a long series of experiments with inoculations of scarlatina, but in the light of modern science they are inconclusive. Some of them were successful, others were not so. Some were made with blood, others with scales of the desquamating skin, but in none was the poison isolated.

Temperature of the Air.—Experience has shown that the poison of scarlatina is affected by temperature. There is a consensus of opinion in the statement that low temperature has no effect, but when the temperature rises to the boiling point of water, contagiousness ceases. This is a very important fact as applied to prophylaxis and disinfection. As a matter of fact, there is no more positive method for destroying the poison than to subject it to the action of boiling water. The action of chemicals upon the poison cannot be accepted with safety. A great number of chemicals has been recommended by manufacturers, and doubtless some do destroy the poison of scarlatina, but until this fact can be proven by scientific observations, it would be futile to discuss the merits or demerits of any of them.

Predisposition.—It can be said that the predisposition of the human race for scarlatina is not so great as it is for some other diseases of the same class. Thus, in Paris Goubert shows the mortality from various diseases, of children under fifteen years of age, to be the following per thousand: variola, 0.793; measles, 0.740; whooping-cough, 0.379; scarlatina, 0.242. This may represent an exaggeration of the relative frequency of these various diseases, as it is known that scarlet fever is not so common in Paris as in the other large capitals of Europe: Berlin and London, for instance. But individual as well as general experience would go to show that variola and measles have greater affinity for the human race than has scarlatina.

Immunity.

One attack protects against any future attacks. Mycelius, quoted by Sternberg, gives the following as the relative frequency with which second and third attacks occur in various diseases:

	Second attacks.	Third attacks.	Fourth attacks.	Total.
Smallpox	505	9	0	514
Scarlet fever	29	4	0	33
Measles	36	1	0	37
Typhoid fever	202	5	1	208
Cholera	29	3	2	34

It will be seen from this that second attacks of scarlet fever are not so common as those of measles, smallpox, typhoid fever, or cholera, as far as the number of cases reported is concerned. Naturally this represents only comparative results, and it would be difficult to represent in figures the ratio of second attacks that exists in these various diseases. The statement can be made that second attacks of scarlatina are rare; indeed, according to the author's experience, rarer than second attacks of measles. As the result of this statement, third attacks must be rarer still, very much rarer than represented in the above table; yet, in looking through the literature of the last few years, it is not difficult to collect a greater number of cases of third attacks than has been done by Mycelius. Indeed, any one with large experience in scarlet fever lasting over a sufficient length of time will have seen at least one case of third attack of scarlatina.

Morbidity depends, as always in infectious diseases, upon a great many factors. The first that seems to be of importance is immunity, and the first question that presents itself is whether any individual is permanently immune to scarlet fever. The only place where this question could be answered by statistics would be in the account of the epidemic that occurred in the Faroë Islands. Here it was shown that after fifty-seven years of freedom from epidemics 38.3 per cent. was affected. This would seem to show that at least a certain number of persons was immune. The figures, however, illustrate more forcibly the tendency to contract scarlet fever than they do the existence of permanent immunity.

In the history of families we find that a certain number remains apparently perfectly immune, that although they may be exposed to scarlatina time and again, these immune members of the family do not become affected with the disease while the other members of the family are affected. Whether this is due to prenatal protection or otherwise, it is difficult to answer. Certainly the protective effect of an attack of angina scarlatinosa has been overlooked in a great many of these apparently immune people. It is very highly probable that with the first epidemic of scarlet fever in the family, all or nearly all the members were attacked by different grades of intensity of fever, the mildest being represented only by an attack of sore throat, not being called scarlet fever at all, and those having had the mild attack of scarlet fever as angina scarlatinosa ever after seem to be immune, while in reality they have had an attack of scarlet fever.

On the other hand, there is that condition that might be called

false permanent immunity. Every one has seen in his experience people who have been exposed a great number of times to the action of scarlet fever and have failed to become infected, and yet finally, after having come in contact with the disease under different conditions, possibly of less resistance or of greater intensity of the poison, they contract scarlet fever in the ordinary way. This is notably the case with nurses who have gone through epidemics of scarlet fever and have remained untouched, and finally, for these reasons or others unexplained, nursing possibly very mild cases of scarlet fever, become infected. Another method of overcoming this false permanent immunity is that of introducing poison by unusual ways into the system. Puerperal scarlatina and surgical scarlatina, both of which are nothing more nor less than an ordinary scarlatina occurring either in puerperal women or in surgical patients, are examples. Von Leube relates his own case as an example of the overcoming of temporary immunity. He states that he had considered himself absolutely immune to the action of scarlet fever, that he had attended any number of cases, that he had seen them in all conditions, under all circumstances, at all times, and yet when he wounded himself in making a post-mortem upon a patient who had died from scarlet fever, he became infected with the poison and had quite a violent attack of the disease. From all this we may judge that scarlet fever does not form an exception to the general rule of the acute infections, *i.e.*, that when the poison is introduced into the system under proper circumstances in sufficient dose, and that poison is of sufficient activity, the result will always be an attack of scarlet fever. The protection that is offered comes to the human race principally as the result of having had a previous attack of scarlet fever. What the prenatal protection is no one can tell positively. At any rate, judging from the results of the statistical investigations in the Faroë Islands, it seems that the human race is more or less protected even in the third generation.

Age.—Temporary immunity is affected, first, by age. The disease may occur at any age; it may be congenital, or it may occur after seventy. It is rare at both ends of the scale. But there is no doubt that the disease does occur after seventy, as can be shown in a great many statistics: Berlin, Norway, Cincinnati, Michigan, and others. Tripe for England has given the following results:

From 1868–72, 2,516,468 died of acute exanthemata: 4.47 scarlet fever, 1.92 variola, 1.85 measles, of the following ages in 1,000:

Age, years	0–1	1–2	2–3	3–4	4–5	6–15	15–25	25–45	45–65
Numbers	65	147	165	149	120	816	22	14	2

Murchison (Jürgensen) pro mille:

Age, years	0–1	1–2	2–3	3–4	4–5	5–10	10–15
Numbers	67	141	160	151	119	259	56

In Berlin from 1875–91 there were 8,622 deaths from scarlet fever:

Age, years	0–1	1–2	2–5	5–10	10–20	20–30	30–40	40–50	50–70
Numbers	406	1,056	3,732	2,747	548	80	38	11	8
In 1,000 deaths	47	122	433	319	63	0.9			

Johannessen for the whole of Norway, total number 9,855:

Age, years	0–1	1–5	5–10	10–15	15–20	20–30	30–40	40–50	50–60	60–70	70–90
Pro mille	103	523	229	48	11	7	2	7	4	3	3
Total	1,019	5,859	2,266	473	117	77	27				

The conclusions that we arrive at as to age are, that the greatest number of cases occurs between two and five years, next between five and ten years, next between one and two years. This seems to be the rule all over the world. In all the statistics that are at hand, whether they come from England, from this country, from Norway, or from Germany, the results seem to be in a broad general way about the same. This has been confirmed by the authors quoted above and verified for England by Richardson, Whitelegge, and Linn, and in a general way by Sanné for France. If we look for the cause for the morbidity at these ages, it will be seen that as in all infectious diseases, when children come in contact more with each other, morbidity increases. Possibly scarlet fever makes an exception to the rule in that the first school years, five to ten, do not seem to be the years in which the greatest number of cases occurs. This may possibly be due to the peculiar manifestations that we find as to the contagiousness of the virus.

Sex.—Of the various statistics collected we find the following:

Murchison.

Below 5 years	51 males.	49 females.
5 to 15 years	About equal.	
15 to 55 years	46 males.	54 females.

Johannessen—49.2 *per cent. Male;* 50.8 *per cent. Female.*

Males.	Females.
1 to 15 years.....19.06 per cent.	1 to 15 years.....19.77 per cent.
15 to 45 years.. ... 1.17 per cent.	15 to 45 years..... 1.97 per cent.

In Cincinnati 1,920 cases occurring in twenty-one years—981 males, 939 females.

There is almost an unanimity of opinion that under fifteen years of age both sexes are affected equally; that after fifteen years (fifteen to forty-five), as is represented in the tables above, the relation is some-

what changed in that there is a slight preponderance of females affected. No adequate explanation of this difference has as yet been given, although the fact that females are more occupied with nursing of the sick has been offered as an explanation why they are more liable to take the disease.

Race.—According to Hirsch, Frich in Baltimore states that the relation of scarlatina, whites to blacks, is as 13.8 to 10.8. In the "Medical and Surgical History of the Rebellion," Vol. III., Part I., we find the number of cases of scarlatina, among the soldiers, was 378 whites with 70 deaths, to 118 colored with 2 deaths. Taking those figures in connection with the relative numbers of white and colored troops, we find that the ratio of morbidity was as 64 colored to 26 white, the mortality being 70 deaths among the white and only 2 among the colored.

In Cincinnati out of 2,764 deaths in eighteen years from scarlet fever, only 11 were of colored people. The results from these three sources seem to vary very much. In the one instance we have a slight preponderance of white over colored affected. In the second we have a percentage more than twice as great among the colored than among the white, and among a large number of cases collected during eighteen years we find that only 11 died among the blacks. It is, therefore, very difficult to answer the question whether race has anything to do with predisposition to scarlet fever. It is probable that there is a difference, judging by these statistics, in predisposition between the black and the white race. There certainly is a difference in mortality as between whites and blacks, but whether this predisposition is in favor of the one race or the other it is impossible to decide.

Social Position and Sanitary Surroundings.—Authors differ very largely in their statements as to the effect of social position and sanitary surroundings upon the morbidity and mortality of scarlet fever. So excellent an authority as Jürgensen claims that there is no difference, that those who live in good social positions suffer as much as those who live under poor surroundings; and those in whom the sanitary surroundings are bad suffer equally with those in whom the sanitary surroundings are good. Upon general principles the poor should suffer very much more than the rich, and indeed this seems to have been the case in some epidemics. But in most epidemics, according to English authors, the rich seem to have suffered equally with, if not more than the poor (Whitmore). Davies of Bristol says the "old and badly ventilated courts enjoy a comparative immunity." Hillier makes the statement that "it has even been asserted by some that this disease proves more fatal to the children of the rich and well-to-do classes than to those of the poor." Prior

makes nearly the same statement. Judging from individual experience, we are justified in coming to the conclusion that upon the whole poor people suffer as little or as much from scarlet fever as do the rich. This is verified if we compare the mortality from scarlet fever with that from measles in hospital practice. In children's hospitals measles is one of the most dreaded diseases. Not so with scarlet fever, both on account of the fact that the latter can be isolated and also on account of the fact that the mortality is as a rule comparatively slight. In order to demonstrate statistically the fact that the poor do not suffer as much, at least not more, the author has had collected statistics of deaths in Berlin for the years 1876–83 inclusive. They have been arranged as to deaths in the cellar, first, second, third, fourth, and fifth floors. In each instance the cellar and the various floors have been considered as to their front and rear apartments.

Cellar.		First floor.		Second floor.		Third floor.		Fourth floor.		Fifth floor.	
Front.	Rear.	Front.	Rear.	Front.	Rear.	Front.	Rear.	Front.	Rear.	Front.	Rear.
392	168	488	355	543	422	590	328	617	396	485	261
560		843		965		918		1,013		746	

It will be seen by looking at the figures that in every instance, whether we take into consideration the cellar or the fifth floor, the number of deaths (reduced to one in the thousand) is smaller in the rear building than in the front building. So that so far as poverty is concerned, mortality from scarlet fever is decidedly less in the poor part of the house than it is in the wealthy part of the house, for in the rear part of the building the rents are very largely below those that are asked for in the anterior part of the building. Comparing the distances from the ground, the greatest number of cases dying seems to be upon the fourth floor, the next greatest upon the second floor. So that as far as these figures go to show anything, they seem to prove conclusively that contact with the earth has nothing to do with the mortality from scarlet fever. Of course, it must always be taken into consideration that fewer people live upon the first floor, in all probability, than live upon the fourth floor. But certainly the number of inhabitants of the first floor is about equal to that of the second or third floor.

Influence of Locality, of City and Country.—The mortality from scarlet fever varies in the most remarkable way if we take into consideration some of the larger cities of the world. Thus, in London there were, during 1868–72, 2,516,468 cases of the acute exanthemata, of which 4¼ per cent. (nearly 115,000) were scarlatina. In five years the number of deaths from scarlet fever in Paris was 67. In Berlin, again, 1877–83, there were 5,428 deaths from scarlatina alone. It

is impossible to say why London and Berlin should be hotbeds for scarlet fever and Paris should be comparatively immune. The fact, however, exists and must be taken into consideration. Just so it is impossible to state why other places upon the globe, as has been shown before and will be referred to immediately, seem to be comparatively immune.

The mortality in cities is really far greater than in the country. It would be better to say that the epidemics of scarlet fever are far more numerous in cities than they are in the country. In cities scarlet fever has almost become endemic, while in the country the number of cases still depends upon the epidemic nature of the disease.

Climate and Season.—It is very difficult to judge of the former. Indeed, the matter requires further study as there are so many apparent contradictions that general conclusions can hardly be reached. Japan and India seem immune. In this country places south of Mason and Dixon's line as well as Southern California are almost the same. The same climates in Europe, on the other hand, present a large mortality, so that one is almost tempted to think of the old view of the *constitutio terræ* of the older writers.

In regard to season, Hirsch has collected reports of 435 epidemics in Norway, Sweden, Russia, Germany, Holland, England, France, Italy, Spain, and North America. Of these 21.8 per cent. were in spring, 24 per cent. in summer, 29.5 per cent. in autumn, and 24.7 per cent. in winter. For London and Sweden the mortality, 1838–53, from scarlet fever can be arranged, as to the seasons, in the following way (Hirsch):

	Spring, per cent.	Summer, per cent.	Autumn, per cent.	Winter, per cent.
London	19.9	25.2	32.1	22.8
Sweden	23.1	23.9	29.4	24.6

Criger reports 1,008 cases of scarlet fever in the *Lancet* for 1891, and there makes the statement that the lowest mortality occurred during the first quarter of the year, there being a slight rise during May, maintained during the summer, and a rapid increase in September, which reached its highest point in October.

The statistics of Johannessen are as follows:

In Sweden, 1867–78, there occurred 65,785 cases of scarlet fever:

January.	February.	March.	April.	May.	June.
11.8 per cent.	9.2 per cent.	9.1 per cent.	7.8 per cent.	7.8 per cent.	6.9 per cent.

July.	August.	September.	October.	November.	December.
6.6 per cent.	6.3 per cent.	5.7 per cent.	8.0 per cent.	10.4 per cent.	10.7 per cent.

In Berlin, 1877–83, there were 5,428 deaths:

January.	February.	March.	April.	May.	June.
6.7 per cent.	5.8 per cent.	5.8 per cent.	6.1 per cent.	7.0 per cent.	8.1 per cent.

July.	August.	September.	October.	November.	December.
8.0 per cent.	8.5 per cent.	10.7 per cent.	13.8 per cent.	10.9 per cent.	8.5 per cent.

It will be seen from this that for Sweden and for Berlin the cold months of the year give the greatest mortality; that upon the whole, however, the fall months are those that produce the greater number of deaths. It is necessary to take into consideration the fact that the terms fall, summer, spring, and winter are elastic, and that what would be a summer season in one part of the world might be looked upon as spring in another, or autumn. In order to decide this question definitely exact meteorological data will hereafter have to be taken into consideration, as the contradictions in statements of authors are so many and so positive that deductions cannot be made with any reasonable degree of assurance.

Pathology and Pathological Anatomy.

Under the heading of etiology we have discussed the general subject of pathology; here it will be necessary to describe the pathological lesions, and at the same time the pathogenesis of some of those that have been thoroughly studied. Again, we must insist that nothing is known of the scarlatinal poison, but that with our present knowledge of lower forms of life much has been done as to their effects upon the human economy; at the same time, cognizance must be taken of the fact that the substances formed as the result of the biological activity of these lower forms of life have also been studied in a limited way. All the lesions of scarlatina are produced by the unknown factor, the scarlatinal virus; by the streptococcus pyogenes, the staphylococcus aureus, or other pus-producers, the bacillus of diphtheria; by the toxins; by one or more or all of these factors in any given individual case. Dissociation is tentative, otherwise we might be able, at least, to arrive at a positive conclusion concerning the effects of the scarlatinal virus.

The skin, as the seat of the most manifest of all the lesions, deserves our first attention. The essence of the changes can be described with Hebra and Kaposi "as hyperæmia with moderate exudation in the normal forms, a corresponding exudation where there are papules and vesicles within the papillæ and the rete Malpighii, and hemorrhage into the papillæ, and the cutis where petechiæ are found." For Barthez and Sanné the lesions of the eruption of scarlatina begin

with the superficial lymphatics and then extend to the capillary blood-vessels. That the lymphatics are very much filled cannot be doubted, but that the process begins within them is an hypothesis which can hardly become anything more when the superlatively intimate relations between blood capillaries and the origins of the lymphatics are taken into consideration. The changes in the skin, however, are of a definite nature; characterized, macroscopically, by swelling, heat, redness; the swelling produced by an œdematous infiltration of the skin, the heat and redness by the overfilling of the blood-vessels, all of which disappear after death, and are therefore of a comparatively transitory nature. Microscopically we find the evidence of a mild dermatitis, extending equally through all the layers of the skin, manifested by dilatation of the blood-vessels, œdematous swelling of the connective tissue, and the presence, in large numbers, of lymphoid cells. According to Wyssokowitch the greatest intensity of the process is manifested about the sweat glands, whose membrana propria seems thickened, the surrounding tissue being much infiltrated with lymphoid corpuscles, and whose ducts are filled with cellular detritus, the result of destruction of the epithelium lining them. After the stage of hyperæmia and œdema, the cellular elements still remain, to a limited extent, and to them there are frequently added large numbers of red corpuscles which have left the capillaries as the result either of diapedesis or of rhexis. The process of desquamation is to be looked upon as due to the direct results of disturbance in nutrition of the older cells of the skin, not to any mechanical uplifting as Sanné thinks. Just as we find nutritional disturbances in all the epithelioid structures, nails, hair, growing teeth, in scarlatina, so do we find them in the skin. As a result of increased function on the part of the apparatuses supplying food to the skin (the lymphatics and the capillaries) each individual epithelial cell runs its life course in a shorter time than normal; therefore the insensible desquamation becomes sensible, and because the nutritional disturbance has been so extensive, therefore the desquamation is extensive in every way.

The process upon the mucous membranes is practically identical with that upon the skin; in normal cases the tongue, the mouth, the tonsils, and the pharynx are principally involved. If we are permitted to judge by the occurrence of functional troubles, especially in the gastrointestinal tract, the conclusion must be arrived at that the enanthem is also developed there as well as upon the parts that can be seen. Wherever an eruption is found, there we find, especially, the streptococcus. The lesions of the mouth and pharynx, as being of so much clinical value, will be described under the heading of symptomatology.

Lymphatic System.—Hawley proposed that the name of scarlet fever should be changed to lymphatic fever on account of the frequency with which the lymphatic system is involved in this disease. As a matter of fact, long experience has taught the author that one of the most constant evidences of scarlet fever is to be found in enlargement of the lymphatic glands. Macroscopically, the changes represent the range from an ordinary lymphatic-gland enlargement to that of an abscess. When the pus-producing agent penetrates through the capsule of the gland, we then have those connective-tissue abscesses that may do so much damage simply by their presence or by erosion of large vessels, producing not infrequently fatal hemorrhage. All the lymphatic glands and follicles may become involved in one or another of these processes. Most commonly it is simple intumescence; this will be found most frequently in the cervical chain (posterior as well as anterior), the submaxillary and parotid group, the glands at the base of the tongue, the axillary and inguinal, and the epitrochlear glands. Abscesses are most common in the submaxillary and parotid groups; not uncommonly they arise within the lymphatic gland that is surrounded by the parotid tissue proper. Microscopically the lesions have been described by Klein, who states that the mononuclear cells are very much diminished in number and are replaced by giant cells or intermediary forms. In the cervical glands he found plugs of fibrin within the veins. Crooke mentions the fact that in the intestine, inflammatory hyperplasia of the lymph follicles is found together with large collections of round cells in the mucosa almost amounting to the formation of pseudo-follicles.

Kidneys.—Hertzka, in reviewing 875 cases of scarlatina occurring from 1871 to 1886 in the Elizabeth Hospital at St. Petersburg, found nephritis in 138 patients (15.7 per cent.). Owen Fowler in 2,000 cases found nephritis in 14 per cent. of all the cases. Johannessen reports that in Norway, out of 36,230 cases occurring from 1873 to 1878 (inclusive), 7,897 had dropsy and morbus Brightii (21.7 per cent.). While these figures are not to be taken as applying to individual epidemics, yet they show the average frequency of renal complications fairly well. Many theories have been formulated as to the etiology of kidney trouble in scarlatina. The oldest is the one claiming that catching cold is at the bottom of all these troubles, as it is indeed at the bottom of all diseases. It is not necessary here to go into a full discussion of this subject; suffice it to say that modern investigation tends to show that other more constant and more tangible causes are at work in every case of scarlatinal nephritis. Owen Fowler has shown that kidney troubles are most com-

mon in summer and states positively that nephritis does not seem to be produced by catching cold, *i.e.*, in scarlatina.

The mutual relation of skin to kidneys is the next theory that must be taken into consideration. As the skin is prevented from excreting, so the kidneys must do more work and therefore will become affected. Opposed to this view has always stood the observation that those cases in which the exanthem is most fully developed are by no means those in which nephritis is liable to occur; so that we cannot accept a simple relation of quantitative insufficiency of the skin function and qualitative changes in the kidney. Furthermore, the nephritis has been explained simply on the basis of a fluxion of blood; at first great hyperæmia of the skin with anæmia of the kidneys and other "internal organs," then anæmia of the skin and hyperæmia of the kidneys and other "internal organs." An intermediary position between this view and the other is taken by Leichtenstern, who claims that the poison is absorbed from the skin, and then, causing stasis in the lymphatics, produces dropsy or inflammatory œdema, and being eliminated by the kidneys, produces nephritis. By movements of the body the lymph current, and therefore the sudden absorption of the poison in larger quantities, is hastened—this explains how getting up too early may favor the production of nephritis. At all events, any view that one may take must presuppose the existence of some body or bodies which should be eliminated by the skin, but are eliminated by the kidneys.

On account of the frequency of nephritis during the desquamative stage of scarlatina, it has been supposed that a real desquamation takes place in the uriniferous tubules. Would that the changes in the kidneys were of so simple a nature! It will be seen further on how complex these changes are, and how comparatively useless the term desquamative nephritis appears to be.

At the present time we seem to have an adequate explanation of the pathogenesis of scarlatinal nephritis. The French school has especially investigated the subject, and various observers (Marie, Haskine, Guinon, Babes) have found streptococci in the kidneys in nearly all the different kinds of scarlatinal kidneys. But while this has been the case in the majority of cases (Babes found it in twenty-six out of thirty cases), there is still left a certain number in which no microorganisms have been found. It seems, therefore, that we must take into consideration another element besides the schizomycetes themselves. This element is the toxic body formed during the living process of lower forms of life. From analogy we are permitted to conclude that when the pathogenic organism of scarlatina has been discovered, it will be found that it also forms a toxin, which,

like all toxins that we know of, produces some change in the kidneys (hematogenous nephritis). For the present, the observation holds good that in all those cases in which there exists an extensive streptococcus infection, we are more liable to have nephritis than in those in which the scarlatinal poison is alone operative.

Klebs, in 1876, first expressed the opinion that in scarlatina we are dealing with a glomerulonephritis. Since that time opinions have varied, but this view has been held to be true in the main. Nearly ten years after the publication of Klebs' article, Friedländer divided scarlatinal nephritis into three classes: (1) Catarrhal nephritis, occurring during the first week of the disease; (2) the large white hemorrhagic kidney, observed especially with severe angina, during the second or the fourth week of the disease; and (3) acute glomerulonephritis, developing after the disease has really run its course. As was found with other forms of kidney trouble, so with scarlatinal nephritis; the conditions are not so simple as to be reducible to a scheme of this sort. It has been stated by one class of observers that the lesion is especially parenchymatous, by another that it is interstitial, and finally that we are dealing with a mixed form of nephritis, as was asserted by Klein as early as 1876. He described the histological changes as follows: The nuclei on the surface of the Malpighian tufts are increased, some of the blood-vessels are closed by emboli, but more commonly there is an increase in the number of nuclei in the walls of the smallest arteries, whose walls seem thickened. Besides this, there is found swelling of the epithelium of the convoluted tubules and proliferation of the nuclei. In the beginning interstitial changes are slight, but after the ninth day they are just as well marked as the parenchymatous changes and consist of round-cell infiltration, starting from around the larger blood-vessels, entering into the base of the pyramids and cortical substance and causing more or less atrophy by pressure. At the same time the uriniferous tubules become filled with lymphoid cells, granular fatty detritus (epithelial), and various kinds of casts. Obliteration of the glomeruli has also been observed. According to Klein, the extent of the parenchymatous nephritis depends upon the degree of interstitial affection, the latter occurring regularly when the patient dies after the ninth day of the disease. Crooke states that even in the first days the kidneys may be found affected, there being marked proliferation of cells or nuclei in the Malpighian tufts, whose capsules, he found, were almost filled. The walls of the arteries were thickened and their lumen was diminished. The intertubular capillaries contained many coagula; here there were also found leucocytes and erythrocytes, the result of diapedesis. The epithelium of

the convoluted tubules was swollen. In all those cases in which death took place after the thirteenth day the nephritis was especially glomerular, but the parenchymatous as well as the interstitial tissue was more or less affected. In this latter instance, it is seen that the claim of a distinctive type of glomerulonephritis for scarlatina is given up. Indeed, as has been abundantly shown, there is nothing peculiarly characteristic to be found in scarlatinal nephritis; as Councilman puts it, as the result of infection depending upon individual predisposition, now one part, at another time another part becomes affected. In the majority of cases we have produced glomerulonephritis, then catarrhal nephritis (parenchymatous nephritis); sometimes interstitial processes predominate, at other times hemorrhagic conditions or even acute suppuration. The essential changes are those of inflammation and degeneration, at no time confined exclusively to either parenchymatous or interstitial tissues, to glomeruli or uriniferous tubules. Yet, upon the whole, it must be conceded that in the majority of instances the glomeruli are affected; if to this there be added certain clinical characteristics we may, joining pathologico-anatomical investigations with clinical observations, succeed in establishing an entity which may be called scarlatinal nephritis. Such an attempt has been made by the writer, as will be seen by reference to the section on Symptomatology.

The Blood.—The changes in the circulatory apparatus are frequently well marked. Reference has already been made as to the blood's containing lower forms of life. The older authorities have contented themselves with the statement that in scarlatina the blood is thinner and less ready to coagulate, that the red corpuscles are diminished in number, and that sometimes urea is found in excess. Modern hæmatology has occupied itself somewhat extensively with this subject, and with a moderate degree of success. Felsenthal and Bernhard have studied especially the specific gravity of the blood, and have come to the following conclusions: In all cases the specific gravity is reduced; the reduction of hæmoglobin is out of proportion to that of the specific gravity (greater). Both the red and white corpuscles are reduced in numbers. In uræmia there is no great reduction in the number of blood corpuscles. Kotschetkow has divided the condition of the blood into three classes in accordance with the gravity of the attacks: the mild, the medium, and the grave (fatal) attacks. In all cases the number of red corpuscles gradually sinks to 3,000,000 per c.mm., or even less, the number not beginning to increase until the sixth week of the disease. There is a marked leucocytosis (from two to five times the normal number of leucocytes); in mild cases 10,000 to 20,000 are found in a cubic millimetre, in

medium cases 20,000 to 30,000 per cubic millimetre, in fatal cases up to 40,000 per cubic millimetre. This increase begins from two to three days before the exanthem, reaches its maximum on the second to third day of the "fluction stadium," and then gradually diminishes, but remains above the normal for a very long time. Intensity of fever, lymphadenitis, otitis, nephritis do not have any influence upon the number of white corpuscles. The percentage of overripe elements—neutrophile and eosinophile cells, is increased in the same way as the number of white corpuscles. In the first two classes the number of these two kinds of cells may be normal or subnormal in the beginning of the disease, gradually increasing until the maximum is reached in the second or third week of the disease (eight to fifteen per cent.), and then gradually coming down to the normal. In grave cases the opposite is observed; the number diminishes with the onset of the disease, and within a few days no eosinophile cells can be found. In the beginning the young elements (large and small lymphocytes) are diminished in number, increasing during convalescence. According to Kotschetkow these changes are so constant that the prognosis can be safely based upon them.

The scarlatinal poison is one that affects the heart with more or less regularity; this can be shown by clinical investigation. In many cases it is simply the nervous apparatus of the heart that is affected. But in very many others the heart itself seems to be the point of attack. Romberg and Hesse have found lesions in the nerves and in the intracardiac ganglia; the former distinct evidences of inflammation, the latter only variations in tinction.

Heart.—In the heart we find diseased conditions in the peri-, myo-, and endocardium. In the *pericardium* we find changes due to inflammation as well as the result of dropsy (hydropericardium). Pericarditis is not uncommon in scarlatina, but is usually only detected upon the post-mortem table. The results of inflammation are found in the exudate, not uncommonly produced by streptococcus or staphylococcus; serum, coagula of fibrin, seropurulent fluid, rarely pus, and still more rarely hemorrhagic effusions. In dropsical effusions the quantity of fluid becomes enormous, so that the heart is practically prevented from dilating by the mechanical resistance of the fluid. Even in the ordinary inflammatory conditions large quantities of fluid may be found, especially when the condition is accompanied or caused by nephritis. Adhesions and consequent synechia follow pericarditis here as elsewhere.

The muscular conditions can be grouped under two headings, according as they are due to histological changes of the *myocardium*, or to changes in increase or tension of the muscular fibres. In the

first instance, we find albuminoid and fatty parenchymatous changes such as are found in the acute infectious diseases. These changes are found very early in the disease; in how far they can be held responsible for those cases in which sudden collapse and death occur is a matter subject to much discussion. It was with some gratification that something more tangible was found in the myocardium of scarlatina patients by Romberg. This observer was able to show that in addition to these changes there were found distinct evidences of interstitial myocarditis in that the myocardial fibres were separated by masses of cells and the arterial blood-vessels showed distinct evidences of inflammation. He found these alterations especially in scarlatina and not in diphtheria. Hesse, while not agreeing to this latter statement, was able to add to the appearances in the blood-vessels that of hyperæmia, hemorrhage, changes in the blood-vessel walls, collections of white corpuscles in their lumen, and perivascular cell proliferation. These changes may lead to chronic myocarditis.

The other class referred to above is that which leads eventually to increase in size of the heart as the result of either dilatation or hypertrophy. Both of them are found in connection with nephritis, and Goodhart was the first to call attention to the relation that exists between acute nephritis and acute dilatation of the heart, although the Germans give the credit to Friedländer, who has done so much in connection with the pathological anatomy of scarlatina. Before Goodhart, Henoch had called attention to the appearance of the heart in scarlatinal nephritis. Jäger states that two-thirds of all the cases of scarlatinal nephritis are associated with cardiac hypertrophy, frequently complicated with dilatation. In thirteen cases he found only one in which there was dilatation without hypertrophy. Goodhart, in his five cases of sudden death in scarlatinal dropsy, found an overfilled left heart. He thinks that during the height of the fever the myocardium has suffered, and when there is added to this a nephritis it is impossible for the heart to overcome the increased resistance. Silbermann corroborates the observations of Goodhart and Friedländer, and explains the cardiac changes as follows: (1) There is no disease in which the elimination of water is so suddenly and enormously diminished as in scarlatinal nephritis; (2) the glomeruli are principally affected; (3) there is such extensive involvement of the kidney structure; (4) the œdema compresses the blood-vessels of the skin, and in this way increases heart pressure; (5) increased resistance in the aortic system is more readily followed by cardiac hypertrophy in children than in adults. If there be, in addition, functional disturbance in the myocardium,

from anæmia for instance, there will be primary dilatation which increases rapidly, instead of hypertrophy with dilatation.

To this there must be added the effect of the toxins upon the heart. We have already noted that the scarlatinal poison has a decided effect upon the heart; if to this effect there be added increased resistance, it is not difficult to explain dilatation. We now know, from observations made in various conditions producing overstrain of the heart, pertussis for instance, that dilatation of the heart may be easily produced; even as the result of prolonged exercise, such as forced marches in soldiers or bicycle riding, temporary dilatation frequently occurs. In children especially is this the case, as the heart yields more readily than in adults, the myocardium being more stable in its internal arrangement in the latter than in the former. The peculiarity of the scarlatinal heart seems to be that hypertrophy takes place in so very short time, cases being on record in which the whole process did not seem to last longer than from one to three weeks, certainly a great exception to the condition we ordinarily expect in compensatory hypertrophy with valvular lesions. This condition is observed especially in children, as that of dilatation without hypertrophy is more frequently found in adults than in children, although Steffen reports six cases in which no consecutive hypertrophy followed dilatation in children. It does not seem unreasonable, from our knowledge in other conditions, to conclude that, as a rule, dilatation in every instance must take place, even if lasting only a short time, with hypertrophy following as compensatory. Clinical investigation, however, must determine this point for us. In these cases the myocardium itself may be normal, fatty degenerated, or even the seat of graver focal lesions, depending largely upon the cause of the dilatation.

Finally, there must not be forgotten those cases of myocarditis in which the lesion of the myocardium is sufficient to produce a dilatation. This condition is the rarest, but nevertheless one that must be distinctly recognized.

The ordinary form of *endocarditis* is the one that is usually found in scarlatina, although many cases of endocarditis ulcerosa have been observed. Endocarditis is a very common complication of scarlatina, but by no means as common as some of the French observers would lead us to believe. The results of the inflammation are usually found upon the margins of the valvular segments, in mild cases small excrescences, in severer ones producing endocarditis verrucosa. They follow the rules of all other forms of endocarditis, being most common in the left heart. Sometimes the lesions disappear, at other times the usual complications of valvular lesions in general develop, or at other times again masses of detached fibrin are washed into the

circulation producing hemorrhagic pulmonary infarcts or embolism of the cerebral arteries. In regard to the pathology of endocarditis there can be no doubt that in the majority of instances it is caused by the various pus-producers: staphylococcus pyogenes aureus, staphylococcus pyogenes albus, streptococcus pyogenes, the bacillus fœtidus (Passet), and others (Klebs, Küster, Weichselbaum, O. Rosenbach, Fränkel, and Sänger). Wyssokowitch and Orth have not been able to isolate lower forms of life in endocarditis verrucosa and endocarditis fibrinosa chronica, and it is more than probable that all cases are not produced in the same manner. Again the action of toxins must be taken into consideration. The discussion that has been going on whether the lower forms of life are brought to the endocardium by means of the blood or the lymphatic circulation cannot be of interest to us; it is sufficient to take the fact into account that microorganisms and toxins do produce endocarditis.

As elsewhere, the lesions are not always localized in one or the other of the three divisions we have made; sometimes the pericardium, myocardium, and endocardium are affected at the same time (pancarditis). Indeed it is difficult to conceive of an endo- or pericarditis that does not affect the myocardium to a greater or less extent, and this must be the case if we take into consideration the peculiar structure of the connective tissue, and therefore the arrangement of the lymphatics, which seem continuous from pericardium on the outside to endocardium on the inside of the heart.

The *gastrointestinal tract* is frequently affected in scarlatina, much more frequently than is indicated by autopsies, although, when the patient dies of the graver forms and early in the disease, evidences of pathological processes are always found.

Reference has already been made to the changes found in the mucous membrane of the gastrointestinal tract. Fenwick has shown that the mucous membrane of the stomach takes part in the general desquamation of the integuments, and that in mild cases, more than severe ones, there is an absolute loss of epithelium. Besides we find great injection and filling up of the gastric follicles with various kinds of cellular detritus. Hesselwarth, in a report of eighty-one post-mortems at the Charité in Berlin, has found twenty-one instances of severe gastroenteritis, and Crooke states that catarrhal gastritis was found in most cases in which it was looked for, and in the severe cases both interstitial and follicular gastritis were found.

In the intestine Virchow showed that the lymphatic follicles as well as those of the omentum were nearly always much swollen. Crooke found inflammatory hyperplasia of the lymph follicles and collections of round cells in the mucosa almost to the formation of

pseudo-follicles; the villi were swollen, infiltrated, and denuded of epithelium. Peyer's patches sometimes presented the appearance found in the first week of typhoid fever.

Wagner, Biermer, and Klein first called attention to the condition found in the *liver* in scarlatina; there is thickening and round-cell infiltration of the connective tissue and cloudy swelling of the hepatic cells; in some cases interstitial hepatitis is well marked and sometimes the round-cell infiltration is intralobular. In both of his communications Crooke refers to the liver; in the first one detailing minutely the changes that occur in this form of hepatitis interstitialis, agreeing with Klein's description and adding thereto the occurrence of focal necrosis. Hesselwarth found hepatitis in twenty out of eighty-one cases.

The *spleen* may be very much affected or normal. When changes do occur, as is the case in most instances, the organ is found enlarged, not infrequently the seat of focal lesions, either hemorrhagic or inflammatory, frequently hyperplastic. Microscopically there are found changes in the blood-vessels: thickening of the adventitia, hyaline swelling of the intima (even to occlusion of the lumen), proliferation in the muscular cells of the media; there is hyaline degeneration in the neighborhood of the blood-vessels, and in the central portions of the Malpighian bodies changes are found similar to those found in the lymph follicles.

The *peritoneum* is sometimes affected, either by hemorrhage into its sac or by inflammation, or the cavity is simply distended with fluid.

All serous membranes may be affected in the same way; the meninges, the pleura, those of the joints; of which further mention will be made in connection with the clinical description of the disease.

Lesions are not infrequent in the *respiratory tract.* These are bronchitis, bronchopneumonia, croupous pneumonia, but they are not distinctive enough to merit special description.

The same can be said of the lesions of the *nervous system,* all or any of which may be found in any infectious disease. The lesions of the liver, the spleen, the serous membranes, the respiratory tract, and the nervous system, on account of the fact that they are found in so many other infections, are probably not due to a special action of the scarlatinal poison. It would be an interesting study to determine what diseases are due to the virus *per se;* unfortunately this, for the present, is impossible.

Symptoms.

The classification of scarlatina is based upon purely clinical evidence, any other basis being, from what has been said, manifestly impossible. We will divide all cases into normal and abnormal scarlatina; meaning by the first term such as represent the average drawn from the observation of a great number of cases; by the second any case which in any way deviates from the average.

In order to study any acute exanthem systematically it is necessary to make certain divisions of the course of the disease, each of which is characterized by one prominent symptom. The normal case will have each one of these thoroughly well developed. Authors differ very much as to the number of the periods, but the following seem to us to offer the best marked boundary lines: (1) The period of incubation, extending from the time of exposure to that of the beginning of symptoms; (2) the period of invasion, which is marked by the subjective or objective manifestations of the activity of the poison; (3) the period of eruption, which extends to (4) the period of desquamation.

We have purposely refrained from going into an historical discussion of the various kinds of scarlatina and the various periods of the disease recognized by the almost infinite number of authors who have written upon the subject. Many of these classifications and subdivisions are too subtle for practical use, some are entirely theoretical, and not a few are absolutely hypothetical and the result of evolution from the inner consciousness of the writers. The divisions we have made will, it is hoped, be found to meet the wants of a practical, working formula. It seems impossible to condense it any more, and extension would only make it indefinite.

Normal Form.

Period of Incubation.

If we take into consideration the various factors that go to determine the length of this period, the various and varying figures to be given regarding it will be readily understood. From an historical point of view it is interesting to note that Trousseau was the first to insist upon a short period of incubation for scarlatina, in which he was quickly followed by Murchison (who asserted that the period might vary from several minutes to five to six days); Richardson reports himself as breaking out with scarlatina while auscultating a scarlatinous patient. The latter observation, like so many of its

kind, is to be taken as showing how careful one must be in accepting conclusions in view of the difficulty of the subject. The factors to be taken into consideration in the study of this subject are the virulence and quantity of the poison, the method of its introduction, and the individual. In regard to these we can only reason from that which is known of the other acute infectious diseases, and therefore possibly no application can be made to scarlatina, as has been pointed out before. That there does exist a difference in virulence of the poison can be proven by reference to the mortality statistics. It would seem rational to suppose that the poison of scarlatina would not behave differently, as regards the human being, from any other poison that we know. In other words, the stronger the poison and the greater its quantity the more rapid and the more intense its effect. So that in the presence of a severe epidemic the period of incubation should be shorter in the majority of cases than it would be in a mild epidemic. Unfortunately, as Barthez and Sanné have pointed out, an epidemic is the worst time to study the period of incubation, as the source of infection cannot be determined with any approach to accuracy.

As has been shown before, one method of introduction of the virus, according to the observers quoted, *the* method of introduction into the system, is by means of the throat. But there are certainly other methods; thus, infection through open wounds, infection in childbed, and probably infection by the respiratory and alimentary tracts.

Under all circumstances it is necessary that the poison gets into the blood where, as Jamieson states, it multiplies rapidly. The period of incubation is that length of time elapsing from the time of exposure until a sufficient quantity of poison has been produced in the circulation to cause symptoms. It will readily be seen how, under these circumstances, this period may vary enormously. Take, for instance, the most common lodgment of the poison, that namely in a crypt or upon the surface of a tonsil; the distance from this surface to the blood is comparatively a long one, if we take into consideration the anatomical structure of the tonsil and its connection with the lymphatics and blood-vessels; especially if there be added the time required for a small quantity of lodged virus to multiply to a quantity sufficient to produce symptoms. On the other hand, a more direct route to the blood than by inhalation can hardly be conceived of, except those taken by surgical and puerperal scarlatina, and for these Lörensen has shown the period of incubation is always short (not to exceed forty-eight hours in thirty-eight cases studied carefully). Paget, Goodhart, Howse, all agree that sudden death on the

second or third day after operation may be due to malignant scarlatina not developed (therefore a period of incubation of twenty-four hours). Trélat and Bókai each report two cases of surgical scarlatina in which the disease developed within the first day after the operation. In most cases of puerperal scarlatina the same condition will be seen to exist. Jamieson states that a longer period of incubation than three days (up to six days) can be possible only when the contagium has lodged itself in the body, but not as yet entered the blood. The study of the period of incubation from this point of view, although presenting new difficulties, would doubtless result in a most important contribution to our knowledge of the disease.

Enough has been said heretofore in regard to individual predisposition. It is sufficient here simply to call attention to the fact that when the poison does enter the blood, according as it may there find sufficient or insufficient pabulum it will develop either very rapidly or comparatively slowly, or, entering sterile blood, not develop at all.

It would be improper to leave the discussion of this part of the subject without at least the suggestion that no critique would be complete without taking into consideration that which might be called the personal equation of the observer. Without impugning the credibility of any one, we may remark that many will consider things proven which to others are theoretical or hypothetical.

From a review of a large number of authors we learn that the following have observed very short periods of incubation: Trojanowsky (24 hours), Loeb (48 hours), Förster (24 hours), Alonzo Clark (several hours), Lotz (45 hours), Ayer (48, 69 hours), Sörensen (in 7 cases under 24 hours), Dukes, Rehn (24 to 48 hours), Gintrac (24 to 36 hours), Salle (32 hours), Raven (12 hours). On the other hand, there are many who have seen cases with long periods of incubation: Trojanowsky (28 days), Hagenbach (3, 7, 11, 14 days), Wertheimber (11 cases 4 days, 6 cases 5 to 6 days, 1 case 2½ days), Vogl (3 to 5 days), Marchand (3 days), Boylan (40 cases, 6 days), Bawy (21 days), Jamieson (5 days), Hamilton (3 days), Dukes (1 to 9 days).

In summing up the evidence, we would state that in the great majority of cases the period of incubation lasts from four to seven days; that next in frequency comes the number of cases in which the time is to be counted by hours, from twenty-four or even less to forty-eight hours, and in the smallest number of cases, always to be examined into most carefully before being accepted, the period is longer than seven days.

Period of Invasion.

The period of incubation is absolutely devoid of symptoms; if the patient is otherwise well, he does not present any evidences of illness until the invasion begins. Suddenly the symptoms begin to develop; more or less malaise, chilliness, decided chills or convulsions, depending upon the age and temperament of the patient, alternating with sensations of heat, a feeling of heaviness in the head to a distinct headache, complaint of tickling sensations in the throat or decided symptoms of sore throat, anorexia, and vomiting. The latter symptom occurs in the great majority of patients, according to Archambault in all children when there is anything in the stomach. Billington saw it in eighty cases out of one hundred and two, while of J. B. Ayer's twenty-three cases only three vomited. The latter is certainly an exceptional experience. The vomited material consists of the contents of the stomach, some mucus, and not infrequently biliary matter. Otherwise the gastrointestinal tract is not affected, constipation, however, being the rule. Depending upon conditions to be mentioned, the patient may be drowsy or wakeful at intervals, but always complaining of being ill.

Examination of the patient leaves the impression of decided illness; the expression is dull, there is great relaxation, no impairment of the sensorium, and decided aversion to activity of any sort. The face is flushed, somewhat fuller than normal, the eyes are dry but dull, very little injection of the conjunctivæ being present, no lacrymation. The lymphatic glands are already enlarged, especially the submaxillary, the anterior and posterior cervical groups, not infrequently the epitrochlear, axillary, and inguinal glands. The spleen and liver vary in different epidemics; not infrequently both are enlarged, but not sufficiently so to be palpated. The tongue is coated with a thin white layer, quite universally distributed, but frequently leaving the edges reddened and with its continuity already disturbed by hyperæmia of the fungiform papillæ, a condition which, when more fully developed, has been erroneously designated as strawberry tongue, especially by American authors. The enanthem is already developing, beginning as a bright red punctate discoloration upon the anterior pillars of the fauces and the uvula and extending very rapidly over the soft palate to the hard palate, covering at the same time the mucous membrane of the cheeks and gums. It is usually thoroughly well developed at the end of the period of invasion. The tonsils are reddened, more or less swollen, and not infrequently partially covered with a whitish, semi-translucent mucus. Alonzo Clark

says there is no scarlatina without the existence of inflammation of the pharynx; it is an integral part of the disease, and an eruption without it is not scarlatina. The temperature runs up rapidly, reaching a maximum at the end of this period, which is rarely below 104° F., and not unexpectedly high when above this. High pulse rates are the rule; there is a disproportion between the temperature and the pulse, which continues for a long time throughout the course of scarlatina and is one of its distinguishing features. A rate of 140 beats per minute need not cause anxiety, even in older children, and in the adult 120 is by no means uncommon at this stage of the disease.

The duration of this period is very short, from six to twenty-four hours; as a rule, the latter approximates the normal condition. Authors vary somewhat as to the time required for this part of the disease to run its course; Barthez and Sanné put it at 12 to 24 hours, even less; Unterberger, 1 to 2 days; Billington, 18 hours; Archambault, 22 to 36 hours; J. B. Ayer, usually 24 hours, the longest 48 hours; Trousseau exceptionally as much as 9 days; Bohn, 12 to 24 hours, sometimes as long as 24 days; Hebra and Kaposi, 12 to 24 hours to 2 to 3 days; Leube, 1 to 2 days; Moizard, 12 to 36 hours, one case in which the eruption appeared upon the sixth day; Albertza, from 2 to 3 hours to 2 to 3 days; the older authors, such as Sprengel and Wendt, all united in asserting that the duration was only 24 hours.

Period of Eruption.

Exanthem.—The eruption begins to develop upon the lower portion of the neck and upper part of the chest, upon the sternum and subclavicular regions. It is characterized at first by discrete, but closely packed, red points, which are slightly elevated but not sufficiently so to be sensible to the touch. Almost immediately the parts of the skin between these points become reddened, but close inspection at first reveals the origin of the redness in the points just mentioned. The skin between these points gradually also changes in color, becoming slightly œdematous as well, so that after twenty-four hours it takes upon itself the characteristic scarlet color, the points of origin becoming slightly pale upon close observation, but the whole looking as if covered with a transparent, non-glistening stain, described by various authors as raspberry juice, minium, the color of a boiled lobster, the color of roses, etc. As a matter of fact, the color varies with the character of the epidemic and the nature of the skin upon which the exanthem develops; it is impossible to describe it in words, and the fact that it is difficult to reproduce is best verified by the many abortive attempts that have been made to represent it in illustrations.

The eruption spreads rapidly, so that by the end of the fourth day the whole body is covered with it. It has been stated that it is characterized by a peculiar reaction upon pressure in that it becomes paler and then the redness begins at the centre and extends to the circumference; any one who will conscientiously try this reaction in other skin troubles will find that it is by no means pathognomonic, but that it will be found in all forms of trouble in which the hyperæmia is especially developed about the openings of the skin glands.

From the upper part of the trunk and the neck the eruption spreads to the arms, the abdomen, the back, and lastly to the lower extremities. It is not found upon the face, as a rule, the latter maintaining the condition described in the period of invasion. When it is developed upon the face, it is found upon the forehead and temples, the cheeks are flushed without an eruption, and the lips and chin are always pale. Upon the extremities it is found with especial intensity where the skin is very thin; therefore, where it covers the places of flexion there is, as a rule, a peculiar intensity of coloration. Upon the backs of the hands and feet it is also well developed, but on account of the richness in sweat glands of the palms of the hands and soles of the feet, notwithstanding the thickness of the skin, the eruption takes upon itself a uniform color, always darker in shade than anywhere else and accompanied by swelling. When the eruption is fully developed, the skin is changed in a way quite characteristic; it feels tense, dry, and, after the swelling has disappeared, like the skin of a corpse, having lost its elasticity as well as its vitality. The eruption remains at its maximum intensity for about three days, varying from one to as much as six or seven days, and then fades in the order in which it appeared.

There are *modifications of the eruption* which can be considered within the normal: scarlatina lævis, which is the special designation of the form already described; scarlatina miliaris, characterized by the eruption of small vesicles, especially well developed upon the chest and back; scarlatina papulosa, in which the original puncta are represented by greater infiltration; scarlatina lævigata, when these puncta are somewhat broadened and seem to reflect the light more than normally; scarlatina variegata, in which there is a difference in the color of the skin about the puncta and the rest of the exanthem, the former being much darker. In some skins slight hemorrhages take place, and under these circumstances scarlatina hæmorrhagica may be considered as not being a deviation from the normal type, although scarlatina hæmorrhagica must, as a rule, be looked upon as an abnormal type of scarlet fever.

Enanthem.—The enanthem develops in the mouth so that by the beginning of the period of eruption it is at its maximum, except, in addition to that which has been described, there is a certain amount of swelling of the mucous membrane of the cheeks, the soft palate, and the gums. The lips are somewhat swollen, dry, and a little later may become fissured and covered with crusts.

The essential enanthematic appearance of this period is to be found on the tongue. Coated as it was during the period of invasion, the fungiform papillæ become more prominent, the tops of the filiform papillæ fall off, and we have a thick, opaque, grayish-white coat, whose surface is dull but even; the redness of the edges increases in area and now the grayish-white coating seems to be lifted off from the tongue (desquamation). It can easily be removed by friction of any sort. At the end of the second to the fifth day we find the tongue absolutely denuded of older epithelium, the filiform papillæ gone, the fungiform papillæ very much injected and swollen, the circumvallate papillæ also swollen. The color of the tongue is red, only intensified by the elevated papillæ; it is slightly swollen, its surface is smooth except for the infiltrated papillæ and may, just after the termination of the process of desquamation, become slightly glistening. We have now the condition of the tongue that has given rise to so much discussion, that has been called the strawberry, raspberry, or cat's tongue. Leube says of it that "when fully developed it is absolutely pathognomonic," a statement that is exaggerated, as there are conditions of the mouth in which this appearance of the tongue is chronic, rare it is true, but in the case of a scarlatiniform eruption making the diagnosis almost impossible. On the other hand, there are normal cases of scarlatina in which the raspberry tongue is not developed at all. Again, the desquamation does not take place so completely as described, and the posterior segment of the tongue remains coated throughout the course of this period of the disease.

The pharynx and tonsils do not present any characteristics differing from those described for the period of invasion. As the region around the tonsils is first invaded, the enanthem runs its course first there; the coating upon the tonsils, which can usually be detected upon close examination, simply represents the process of desquamation, which can be seen where the mucous membrane is not too much disturbed by movement.

The *temperature* curve, as an average, is fairly characteristic of the disease; it may be represented by the chart on page 42.

It will be seen from this that the fever is a febris continua for the period of eruption; marked by high morning and evening temperatures, rarely below 104° F., and that under normal circumstances

the high temperature lasts from four to five days. The temperature falls by lysis, and the first break comes on the sixth day of illness. Variations in normal cases are as follows: The temperature does not reach 104°–105° F. as a maximum, but reaches 102° or even a little less; the fall is more rapid than indicated in the curve, so that it

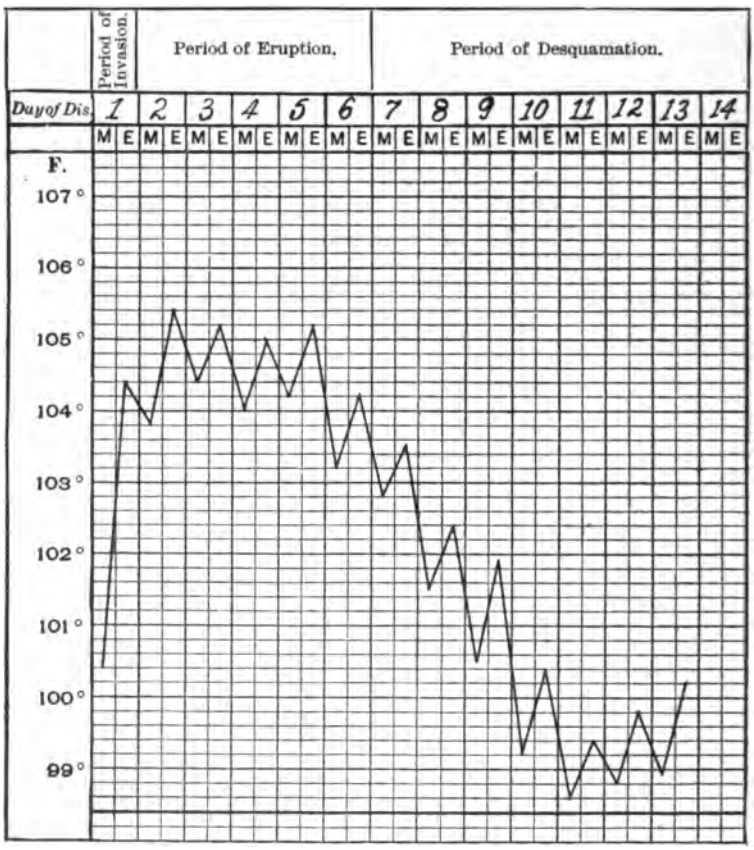

FIG. 1.—Chart Showing the Temperature Curve in a Typical Case of Scarlet Fever.

sometimes approaches the type of a crisis with subnormal temperatures. Again the first maximum may be followed by crisis or lysis or there may be typical typhoid, step-ladder increase from the beginning until the maximum is reached (three to four days—Vogl). Henoch notes in a review of 175 cases, 4 with normal morning temperatures and high evening rise. Litten has seen the same; he also notes some cases with high initial fever followed by an afebrile course. Jamieson in a report of 200 cases before the Edinburgh

Medico-Chirurgical Society gives the maximum temperature as follows: In 11 cases on the first day; in 76 cases on the second day; in 75 cases on the third day; in 36 cases on the fourth day; in 2 cases on the fifth day.

As a rule the height of the temperature is significant as indicating the intensity of the attack, although some of the most malignant forms are associated with subnormal temperatures.

The pulse is rapid throughout the course of this period. Sometimes the ratio between respiration, temperature, and pulse is maintained, but more frequently the pulse is more rapid than would be warranted by the elevation of temperature.

The enlargement of the lymphatics and spleen, noted in the previous period, remains the same.

The *urine* either shows the ordinary evidences of febrile urine or there may be febrile albuminuria beginning with the second or third day and lasting to the sixth and seventh (Jaccoud). Centrifugated, the urine shows cylindroids and degenerated epithelium, rarely casts or blood corpuscles. Binet found albumin in thirty-four cases out of forty-three. Stevenson has found it in sixty per cent. of all cases of scarlatina, and Eisenschitz thinks albuminuria as much a part of scarlatina as a cough is of measles. Peptonuria has been looked upon as characteristic of scarlatina; for further details see the section on Nephritis (page 61).

During the period of eruption the patient is affected differently according to the individuality. The symptoms are produced principally by the fever, the eruption, and the sore throat. There is present loss of appetite, constant thirst, somnolence with delirium, or, on the other hand, restlessness with more or less nervous manifestations. The patient complains of dryness of the mouth and throat, tickling or pain, especially in swallowing; the glands at the angle of the jaw now are decidedly swollen and frequently painful on pressure. The eruption causes more or less irritation, burning, smarting, and itching, and frequently increases the restlessness of the patient.

The *bowels* are either constipated or loose; diarrhœa at this period of the disease is not to be looked upon as of any special import, unless the number and character of the stools tend to affect the patient. Not infrequently urine and stools are passed involuntarily, although the patient knows that the acts are about to be performed or have been done; so that we have the condition seen so often in febrile conditions in which the sensorium is perfectly intact during wakefulness but not sufficiently inhibitory during sleep.

The *respiratory apparatus* is singularly free from diseased conditions; there may be a slight seromucous discharge from the nose,

but even this must be looked upon with suspicion. There may be present a dry, more or less hacking cough, but this is due to the irritation of the throat.

Period of Desquamation.

Under normal conditions the desquamation begins where the eruption first made its appearance, *i.e.*, upon the neck and upper part of the chest. It varies in character, according to the intensity of the attack, as far as the general symptoms are concerned, to the histological structure of the skin, and also to the individual structure of the skin. There are those in whom a most moderate amount of eruption is followed by desquamation, so severe that it produces very intense local symptoms; on the other hand, in others very intense desquamation is accompanied by no irritation. To the former class belong those in whom the slightest amount of local irritation produces dermatitis, those whose skins are easily affected by insect bites, thermal or chemical irritants, or whose skins are subject to eczema of non-constitutional origin.

The desquamation, when observed, is preceded by the peculiar appearance already described as occurring at the end of the period of eruption. It begins in one of several ways: upon the neck and trunk either in the form of small circular elevations developed upon the original puncta, or in the form of epithelial fissures more or less regularly arranged according to Langer's spaces, or without reference to these. The circular elevation looks almost like a vesicle, but careful inspection will show that it is simply a small disc made up of dead epithelium; from these puncta as starting-places, the skin begins to be shed in all directions until the small desquamating circle meets other circles starting from other puncta, and in this way all the old skin is gradually removed. The method by fissures is more readily noticed than the one just described, but is not so common, and for this reason the statement is so frequently met with that desquamation is rudimentary. In this method the skin looks almost like that of ichthyosis and the scales fall off as in the other method, in small particles which are found floating upon the surface of the water used for bathing. The third method is simply a rudimentary development of the second.

Upon the face the desquamation is furfuraceous; it can hardly be called scarlatinal desquamation, but is the same as might occur in any condition in which there has been so much congestion of the skin. As a rule it is absent, occasionally it happens that genuine desquamation does occur about the forehead and temples. Upon the lower segment of the trunk, the arms, and legs desquamation takes

place in lamellæ (desquamatio membranacea); this begins usually by a fissure in the dead epithelium, and then the skin strips off or is pulled off in long membranes. The author has in his possession a strip of dead skin that represents the whole covering of the anterior aspect of the forearm. But desquamation here may also be furfuraceous.

The most characteristic desquamation is found upon the palms of the hands and soles of the feet; it begins last upon these places, usually upon the ball of the thumb and immediately under the nails. In the latter place there develops a fissure, beginning where the nail is attached firmly, and then the skin strips off always according to the lamellar type, never the furfuraceous. This is the only place upon the body where the type of desquamation is always the one kind, never mixed nor furfuraceous. It is not uncommon to find casts of the fingers or toes taken away, but usually the patient does not allow these casts to form.

In some cases desquamation is exceedingly rudimentary and must be looked for most carefully before it can be detected.

It is impossible to describe the desquamation as it may occur in any one individual. It has been shown that, although subjected to the influences mentioned before, desquamation may take place in regions upon which there has been no eruption, and that the most violent exanthem may be followed by rudimentary desquamation, and the reverse; but upon the whole, the more violent the general symptoms are in the beginning the better marked is the desquamation, and the better marked the development of the original puncta is the better marked is also the desquamation.

It is not only the skin that is affected during this period, but all epithelial tissues—the hair, the nails, and the teeth. The hair breaks off after scarlet fever, the nails always show indentations and sometimes are shed, and the forming teeth are more or less affected, usually by lack of enamel deposit, sometimes in the deeper structures.

The *temperature* now begins to fall, as shown in the chart on page 42; with it, but usually one or two days later, there is a fall in the pulse rate. With both of these there is a marked change in the appearance of the patient; not uncommonly there follows a prolonged sleep, otherwise the appetite remains, thirst disappears, the exanthem and the changes upon the tonsils gradually grow less and less until the tongue is again covered with epithelium and the tonsil is reduced to its normal size. The lymphatics come back to their normal condition, the hæmoglobin in the blood is gradually increased, the urine is neither albuminous nor febrile, and by the end of the second week it is with difficulty that the patient is kept in bed.

The period of desquamation lasts from two to four weeks. Unterberger gives the period as from two to five weeks; Thomas from several days to several weeks; Barthez and Sanné state the average to be from one to three weeks, and Bohn says that it lasts two, four, six, and eight weeks.

In normal cases the prognosis is absolutely favorable, the end is always *restitutio ad integrum*. The disease runs its course, and by the time desquamation is completed the patient is as well as he was before the attack, ready to take up his occupation and to be treated as perfectly well.

Abnormal Forms.

Under this heading come those cases in which there is either lack of development or too great development of such symptoms as belong to the normal cases or in which complications are added to these normal symptoms. The classification that we would make is then as follows:

I. Rudimentary forms;

II. Grave excessively developed forms;

III. Complicated forms.

It has always seemed to me a waste of time to discuss classifications, as, after all, they only serve a temporary convenience. In the above subdivisions it will be seen that the term malignant as being too elastic as used, has been discarded. No well-marked line of demarcation can be drawn between malignant and grave forms. Malignancy may be due either to the scarlatinal poison or to complications; but as the poison of scarlatina has not been isolated, it will be better to omit the term entirely from a classification.

Rudimentary Forms.

Rudimentary forms are those in which one or the other period of the disease is imperfectly developed. It will be seen that as each period has its cardinal symptoms, the clinical description will hinge upon the rudimentary development of these. In the period of invasion we sometimes find an entire absence of symptoms. The duration of the period may be very short, only a few hours, and then of course there can be no symptoms of any magnitude. An afebrile period of invasion probably occurs very frequently, at all events there is often such an utter lack of evidence of sickness that it is overlooked. The symptoms of gastric derangement may also be absent. But the most important lack of development will be found in the enanthem. Some-

times this is only badly developed, possibly a little redness of the pharynx, or the pillars of the fauces, without much involvement of the lymph glands, not even the scarlet fever tongue shows itself in a sufficiently characteristic manner to be conclusive, or there may be no enanthem at all. The tonsils in the latter condition are not enlarged, and this condition may persist throughout the whole course of the disease when there is developed that form which has been called scarlatina sine angina.

In the third period the exanthem is the symptom that shows most variations. It may be very rudimentary, not characteristic in its development, lasting only a few hours, resembling an ordinary erythema, or a pressure spot, or the redness due to fever. Or the exanthem may be entirely wanting, scarlatina sine exanthemate. In these cases there may be a rudimentary enanthem, again not sufficiently characteristic, or it may be well developed. In them the diagnosis can be established only by taking into consideration the antecedents and the surroundings of the patient. These cases are apt to occur in connection with a widespread epidemic in persons little susceptible to scarlatinal poison or in such as have had scarlatina in childhood. It is frequently found in adults, is not uncommonly overlooked, and is often the cause of the spread of epidemics. In former days of bad sanitation it was not an uncommon experience to find various types of the disease represented in one family, the elders simply having scarlatina sine exanthemate, the whole disease being represented by a form of angina that was called nurses' sore throat. As there are people who cannot nurse diphtheria without getting nurses' sore throat, which upon bacteriological investigation proves to be diphtheria, so there are others who cannot nurse scarlatina without suffering from sore throat which, if we could isolate the cause, would sometimes undoubtedly prove to be true scarlatina. When the scarlatinal tongue develops in these cases, as it does in most instances but not always, the diagnosis is made easier.

The fever may be so slight as not to call attention to its existence; when measured with the thermometer it does not go above 101° F., lasts for a few days, and then disappears entirely. With this the general condition of the patient does not show any evidence of illness; the appetite continues good, digestion is unimpaired, and the patient rather ridicules the idea of being treated.

The duration of this period may be only twelve to twenty-four hours, and of course is then overlooked, or it may be a few days. For the sake of the patient, as well as for the sake of the surroundings, the treatment must be the same as that of any other case of scarla-

tina, for not infrequently cases of this class develop into a complicated form, renal trouble sespecially occurring.

The period of desquamation may be marked by a lack of scaling or by desquamation not characteristic of scarlatina. Desquamation may be absent altogether, or it may l t only upon certain parts of the body, the elbows, the knees, of the hands, and the soles of the feet h he most com s for desquamation in rudimentary fo the desq ay not be lamellar at all, noticeable e water c ub, furfuraceous s only in sp from it t s is impossible.

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These cases may be rudimentary also, and in two ways: in that the patient does not live long enough to dev[illegible] the symptoms of the various periods, or in that the sym[illegible] the part of on[illegible] apparatus so dominate the whole clinic[illegible] that either others are lost sight of or actually do not[illegible] The charac[illegible] istic feature of this class of [illegible]es is the i[illegible]f the ner[illegible] system. Post-mortem e[illegible]on revea[illegible]n the ce[illegible] nervous system, and th[illegible]le, only [illegible]he brain [illegible] stance, injection of the [illegible] overfilli[illegible]entricles [illegible] addition there are found [illegible] already [illegible] conne[illegible] with the myocardial lesi[illegible]mptatic[illegible] exclud[illegible] such cases from this clas[illegible] listinct[illegible]ry les[illegible] exist, these being due to [illegible] of lov[illegible]ife [illegible] than that of scarlatina; aga[illegible]nclus[illegible]enta[illegible] Leichtenstern thinks that th[illegible]ptor[illegible] œdema of the brain, caused [illegible]y th[illegible] and has classified them as foll[illegible]

Coma—due to œdema and anæmi[illegible]
Convulsions on one side—due to [illegible]
centres (unilateral) or their co[illegible]
Headache—due to [illegible] and anæm[illegible]
Tachypnœa and [illegible]—due t[illegible]
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General convuls[illegible]
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Bilateral amauros[illegible]
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tina, for not infrequently cases of this class develop into a complicated form, renal trouble sespecially occurring.

The period of desquamation may be marked by a lack of scaling or by desquamation not characteristic of scarlatina. Desquamation may be absent altogether, or it may be present only upon certain parts of the body, the elbows, the knees, the palms of the hands, and the soles of the feet being the most common places for desquamation in rudimentary forms. Or the desquamation may not be lamellar at all, noticeable only in the water of the bathtub, furfuraceous and then only in spots, so that from it the diagnosis is impossible.

Lastly, we must call attention to a rudimentary form which is supposed to exist and in which none of the symptoms of scarlatina are present, but in which the only manifestations were gastroenteritis or nephritis. Leube remarks, and justly, that until the scarlatinal virus is isolated, our judgment in regard to the nature of these cases must be withheld.

As a résumé of the anomalous rudimentary forms without complication we have made the following table:

Period of Invasion.	Period of Exanthem.	Period of Desquamation.
Normal.	Rudimentary or absent.	Normal.
	Rudimentary or absent.	Rudimentary or absent.
Abnormally long or Abnormally short.	Normal.	Normal.
	Rudimentary or absent.	Normal.
	Rudimentary or absent.	Rudimentary or absent.
Without enanthem.	Normal.	Normal.
	Rudimentary or absent.	Normal.
	Rudimentary.	Rudimentary or absent.
Afebrile.	Normal or afebrile.	Normal.
	Rudimentary or absent, with or without fever.	Normal.
	Rudimentary with or without fever.	Rudimentary or absent.

Excessively Developed Forms.

This division must of necessity be tentative, as it involves only those cases that are excessive on account of the quality or quantity of the scarlatinal virus taken into the system. In the vast majority of cases, as has been repeatedly pointed out, the excessive development of symptoms is due to the streptococcus pyogenes; but, as Fränkel and Freudenberg state, some of the malignant cases of scarlatina owe their malignancy not to the streptococcus but to the scarlatinal virus. We would then consider only those cases as belonging to this class in which it is fair to suppose that the localization of the virus has produced the grave symptoms—a task both diffi-

cult and fraught with a certain amount of risk, in that the discovery of the scarlatinal poison and its properties may overturn all our concepts of the present.

These cases may be rudimentary also, and in two ways: in that the patient does not live long enough to develop all the symptoms of the various periods, or in that the symptoms on the part of one apparatus so dominate the whole clinical picture that either the others are lost sight of or actually do not develop. The characteristic feature of this class of cases is the involvement of the nervous system. Post-mortem examination reveals lesions in the central nervous system, and then, as a rule, only œdema of the brain substance, injection of the meninges, overfilling of the ventricles; in addition there are found the changes already described in connection with the myocardial lesions. The temptation exists to exclude all such cases from this class in which distinctly inflammatory lesions exist, these being due to the presence of lower forms of life other than that of scarlatina; again, here, a conclusion would be tentative. Leichtenstern thinks that the cerebral symptoms are due to localized œdema of the brain, caused by irritation by the scarlatinal poison, and has classified them as follows:

Coma—due to œdema and anæmia of the anterior cerebral lobes.
Convulsions on one side—due to œdema and anæmia of the cortical motor centres (unilateral) or their conducting fibres.
Headache—due to œdema and anæmia of the meninges.
Tachypnœa and tachycardia—due to œdema and anæmia of the medulla oblongata.
General convulsions—due to œdema and anæmia of the pons or cortical motor centres (bilateral).
Bilateral amaurosis with pupil reaction intact—due to œdema and anæmia of the posterior lobes of cerebrum, corpora quadrigemina.

In describing these cases we must, for the sake of simplicity, discard the method employed in the other two forms, because subdivisions cannot be made here with profit and individual types run their course in peculiar ways. Only one kind has all the periods thoroughly well developed, and this form is really the one that has prompted us to make the subdivision we have made. It can be called the excessively developed form *par excellence* and is characterized by an increased development of all the normal symptoms. The fever curve, taken from one of my patients, a little girl aged six years, when compared with the normal curve will show how this symptom is exaggerated.

In this patient every symptom was exaggerated; it will be noticed that, with the eruption on the second day the temperature rose to

106° F., remaining between 105° and 107° until the morning of the sixth day, when there developed a lysis ending in a practically normal temperature on the twelfth day, but really showing slight elevations until the fifteenth day. The enanthem and exanthem were the most violent in regard to intensity and extension that could be imagined; there were present miliaria, which became confluent and in places

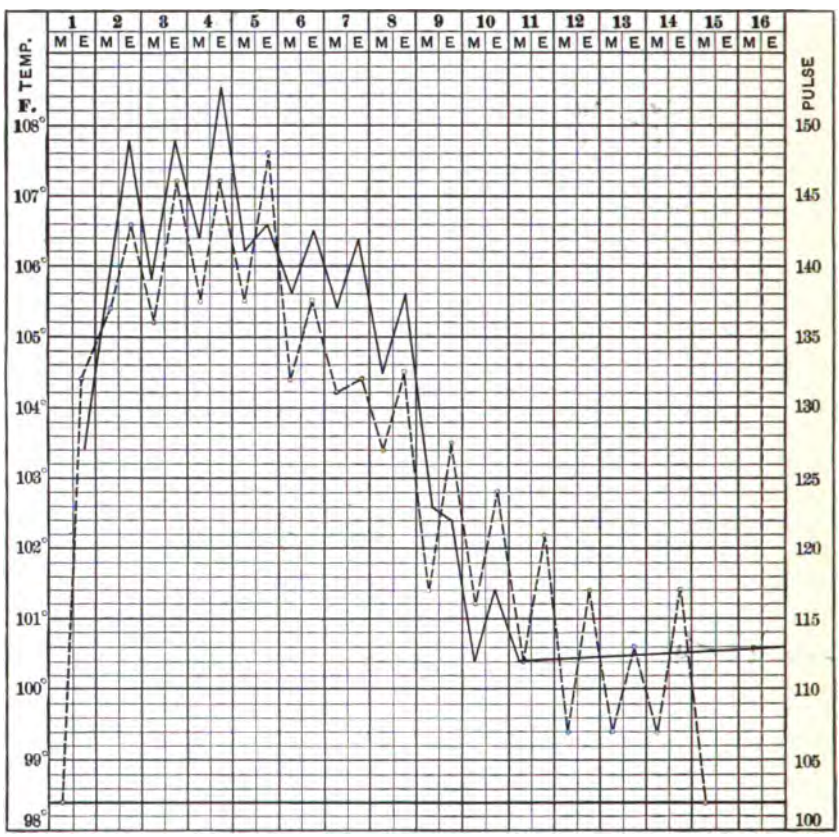

Fig. 2.—Chart Showing the Temperature Curve in an Excessively Developed Form of Scarlet Fever. The dotted line represents the temperature, the continuous line the pulse curve.

resembled the vesicles of herpes. During the period of the eruption there was constant delirium, jactitation and wakefulness relieved only by hydrotherapy, and followed on the beginning of the sixth day by a comatose condition which lasted for over forty-eight hours. The pulse was very rapid, as will be seen by the chart, but as it fell with the temperature it seemed that the synchronous action of the important nerve centres was not disturbed, and, as a matter of fact,

after the eighth day the child made a perfect and uninterrupted recovery. No more exquisite condition of enlarged lymphatics could have been observed in any disease; both the liver and spleen were also enlarged. During the period of desquamation there developed intertrigo and fissures going into the corium in various parts of the body. The strawberry tongue was developed to its most perfect condition, the tongue looking as red as an unbroiled beefsteak. There was febrile albuminuria, but no evidence of renal trouble beyond this. But with all this, there was not a single complication, simply an excessive development of all the symptoms.

Most of the forms in this class are, unfortunately, rudimentary; it is rare to have a case go on to recovery, usually the result is death. The fatal termination most commonly occurs in the period of eruption, next during the period of invasion, and most rarely does the patient live to enter into the period of desquamation. They all have the same general characteristics, the symptoms varying with the individual and the end coming as the result of paralysis of some vital nerve or nerve centre, or changes in some vital organ, especially the heart. By some it has been supposed that in death by the heart the vagus or its centre is affected, as in diphtheria; death due to profuse diarrhœa is supposed to be due to some lesion in the splanchnic nerves (Henoch); the former view has been discussed in connection with pathology; the latter has found no verification as yet. What rôle is played by the so-called status lymphaticus, called into consideration in connection with scarlatina especially, must be determined by future investigations; the theory is very enticing but as yet not sufficiently worked out in practice. Up to the present pathological anatomy has not given us sufficient data to explain the virulence of these attacks; this should not be asked for, however, as the mechanism is the same as in any other severe acute intoxication; no one asks of the pathologist an explanation in case of fatal strychnine poisoning, and these cases must be looked upon as instances of fatal scarlatinal poisoning without lesions appreciable to our present modes of investigation, all of which will become clear after the physiological effects of the scarlatinal poison shall become known.

The most rudimentary form is that in which death occurs during the period of invasion or in the beginning of the third period—such cases can properly be called foudroyant. The most common symptom is the high temperature, which occurs in all these cases when there is no complication. The patient is taken ill with high fever, temperatures of 110.5°–111° F. being on record. With this there may or may not be vomiting, the enanthem may or may not be present; it is absent especially in those cases that run a very short course. Diar-

rhœa is also a symptom in some of these cases. The pulse is very high from the onset, 120–160 and frequently above, sometimes small, sometimes bounding and full, becoming irregular, intermittent, sometimes even slow. In a short time the symptoms on the part of the nervous system begin to develop. First headache, then delirium, which is violent but passes rapidly into a stage of somnolence, and this is again quickly followed by coma, usually very profound, sometimes coma vigil or alternating forms. During the stage of coma convulsions may develop, partial or general; the urine is retained or, with the fæces, is passed involuntarily; and death comes, pulse, temperature, and respiration going higher and higher, the Cheyne-Stokes respiration and type of pulse developing, until both pulse and respiration cease, sometimes one first, sometimes the other.

When the fatal termination does not come so soon a typhoid condition may develop, characterized by dry tongue and mouth, a certain amount of meteorism, small pulse, cold extremities, and finally collapse. If the eruption develops at all in these forms, it is either rudimentary, appearing and disappearing in a very short time or it may be developed in the most irregular way, possibly upon the extremities and not upon the trunk, frequently as scarlatina papulosa or variegata, always with a tendency to cyanosis. These patients live from eleven hours (Trousseau) to forty-eight hours. Hemorrhages are not common, this symptom being especially developed in cases of streptococcus complication; but they may occur from any of the mucous membranes, petechiæ may develop or the eruption may be hemorrhagic in character.

The most common form is that in which the whole condition lasts from three to five days into the period of the eruption. The period of invasion in these cases may be normal or as in the foudroyant cases. In the first instance the nervous symptoms appear upon the second or third day of the eruption, this latter stage developing normally; the writer has seen it thoroughly well established in every regard, when the temperature, pulse, and respiration began to rise, the eruption disappeared, not all over the body and in the normal sequence, but remained in patches, larger or smaller, possibly cyanotic or even petechial, and then the nervous symptoms described before developed. Sometimes the condition of scarlatinal typhoid (so much made of by German authors) develops, which may last for some time but finally ends fatally.

At other times the period of invasion is abnormally excessive, accompanied by incessant vomiting and diarrhœa, well marked angina, but no patches; the eruption appears in an abortive way,

bronze colored, cyanotic, even hemorrhagic, the condition goes from bad to worse and in a short time ends fatally. Another variation is the one in which the evidences of nervous trouble cover over all the others—a condition like meningitis marking the period of invasion, so much so that Laveran considered cerebrospinal meningitis a form of scarlatina. This may continue for five to eight days, then the eruption appears followed by desquamation. Death occurs with all the symptoms of meningitis, but post-mortem examination shows nothing more than circulatory disturbances in the meninges.

Lastly there must be considered that form which has been called the *adynamic*, and which tallies very closely with the description of cases supposed to be due to the status lymphaticus. The dominating symptom is weakness, muscular and otherwise, the fever is high, but not abnormally so, the pulse is small, easily compressed and weak, there is stupor almost from the beginning. The eruption makes its appearance normally, but the general symptoms increase; we have subsultus tendinum, fibrillary muscular contractions about the face and eyes, and delirium during sleep. Sometimes vomiting and diarrhœa persist throughout the course of the disease. The strength of the patient fails; it is impossible to give nourishment, stimulants are rejected by the stomach; on account of the lack of tonicity of the blood-vessels and lack of nourishment in the vasomotor nerves, bedsores form, and the patient, losing day by day, finally dies in a condition of extreme debility. Sometimes here also a typhoid condition develops, and, indeed, in the beginning, especially in very young children, it is difficult to state positively that we are not dealing with typhoid fever.

Complicated Forms.

The most common complication is that of streptococcus infection. The streptococcus affects very many organs in the body; but it is not the only lower form of life that causes complications, as has already been shown; nor, tempting as may be the theory, are lower forms of life the only complicating agents. It would be pleasant to undertake the task of describing this form from the etiological point of view, and, doubtless, in the future this will be the method that will be adopted. Since this is not feasible as yet, we shall describe the complications as they arise in the various organs and systems; in this way, it is to be hoped, a better clinical picture can be obtained than by adhering to the method employed before.

Complications.

The Throat.

The most common form of complication is to be found in the throat. Two conditions can be distinctly recognized here, the one occurring at the beginning of the disease or developing before the end of the first week; the other developing during the second or third week. The first form is as a rule a streptococcus infection, although staphylococci and the bacterium coli commune are found. Upon the whole it can be stated that the angina of scarlatina is in most instances a streptococcus infection. In a large percentage of cases this is the form of sore throat that we have to deal with; in other words, no Löffler bacilli are found. Selner has found Löffler bacilli present in two per cent. of scarlatinal sore throats; and in six hundred and sixty-four cases Thure of Hellstroem has come to the same conclusion. The second form is usually true diphtheria, although here again sometimes streptococci are found exclusively. To the first form the term primary angina has been applied; to the other, secondary, although it would be more exact to speak of pseudodiphtheritic angina, or, better still, to denominate the angina by the form of lower life that is found. The Klebs-Löffler angina cannot be taken up here. Its history is practically the same as everywhere else, varying only according to the condition the patient had been left in as a result of his previous attack of scarlatina and the method of treatment.

For the *streptococcus angina* the conditions vary from comparative harmlessness to absolute fatality. Some authors have made three forms of streptococcus angina: the erythematous, the pseudomembranous, and the gangrenous. Like all classifications, this is only valuable to a certain extent, for we have one form running into another. A case may begin as an erythematous form and end as a gangrenous form; we may have upon the one side an erythematous form and upon the other a pseudomembranous form.

The appearance of the throat in the *erythematous form* is such that the enanthem seems simply to be reinforced, so that from a clinical point of view this form of angina must be looked upon as coming within the normal appearances of scarlatina.

The *pseudomembranous form* begins as follows: The membrane appears upon the tonsils, gray, glistening, not very opaque, at times looking as if the mucous membrane had been covered by a thin opaque varnish. Attempts to brush or peel it off are followed by denuda-

tion, leaving a bleeding surface. In the majority of instances the membrane is confined to the tonsils, becoming thicker, less glistening, and in no way to be distinguished from a true diphtheritic membrane. This condition may last three to five to eight days or longer. Gradually the membrane comes away, the tonsils are left red, possibly swollen, and as far as the local process in the throat is concerned, *restitutio ad integrum* takes place. With this attack there comes an increase in temperature and pulse. But these cases are accompanied by something of very much more importance—enlargement of the lymphatics, which may in due course of time lead to very important and sometimes serious complication.

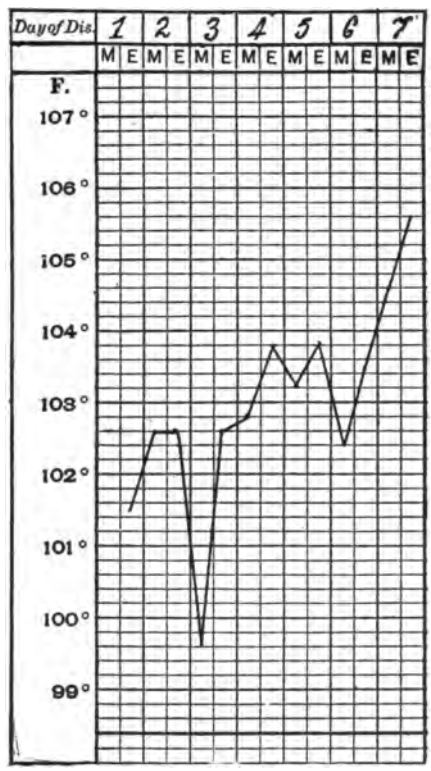

FIG. 3.—Chart Showing the Temperature Curve in a Case of Streptococcus Angina with Low Temperature. The patient was a boy, seven years of age, who had cerebral symptoms, a rapid pulse, and albuminuria. Death took place on the seventh day.

Under other circumstances the course of the disease is not so simple. The membrane begins to spread to the soft palate, upon both its anterior and posterior aspects, in very severe cases spreading anteriorly over the tongue, the mucous membrane of the cheeks, and upon the lips and gums; posteriorly spreading into the nares or into the Eustachian tubes, producing clinical pictures that require further description. Under all circumstances with this intense development of the membrane we usually have constitutional symptoms that warrant an assumption of gravity in the course of the disease. The fever becomes very high, the pulse rate very high, symptoms on the part of the nervous system, stupor, delirium, and coma, follow, the patient becomes adynamic, the urine contains albumin, and locally there is always great intumescence and enlargement of the lymphatic glands depending upon the part that is affected. In other cases the fever is moderate as shown in the accompanying chart. Localization in other parts, the spleen, the kidneys, the heart, occurs

as in every other form of sepsis. Leichtenstern reports a very violent epidemic occurring in the hospital at Cologne, in which there were 467 cases with 108 deaths, the mortality being 23 per cent. In this epidemic scarlet fever was complicated by diphtheria and measles. Diphtheria occurred in nearly four-fifths of the cases, sometimes late in convalescence. Among some of the septic complications that he mentions are: In two cases there were corneal ulcers, in one case hypopyon keratitis, in one case there was choroiditis, which ended in phthisis bulbi; in one case cellulitis began in the neck and extended to the umbilicus. Furthermore, especially in children, purulent mediastinitis, pleuritis, pericarditis, late adenitis, and periadenitis were remarkably concurrent with nephritis. Perichondritis and necrosis of the cartilages were noticed in two fatal cases, sometimes lobular or lobar infiltration of the lungs and purulent pleuritis; so that it will be seen that the statement made above is within the limits of actual observation.

When the membrane spreads to the nose, breathing is impossible through the nose, there follows a sharp acid discharge, which produces an artificial eczema or even ulceration upon the upper lip. The odor becomes extremely offensive, and the patient, lying there comatose with this ichorous offensive discharge rolling over the lips, continually losing strength, soon succumbs to complications in vital parts.

Again, this condition of sore throat may give rise to all the symptoms of a cryptogenic septicæmia with all its various complications, pus-producing inflammations in almost every organ in the body, and it may do not a little to change a condition that apparently was benign into one that is malignant.

Lastly, in connection with the extension of the membrane, the fact must be borne in mind that the membrane sometimes, rarely it is true, extends into the larynx and produces true croup. In other words, it is not necessary that a membrane be diphtheritic in order that the symptoms of croup develop, as has been shown by numerous bacteriological investigations.

Ears.—When the disease spreads into the Eustachian tube, middle-ear abscesses or internal-ear troubles follow, giving rise to a long-continued discharge, sometimes lasting for years, followed almost universally, when left to itself, by deafness; or more serious complications may happen in the way of extension to the meninges, thrombosis of veins, and cryptogenic septicæmia. When extension has taken place to the middle ear, unless the sensorium of the patient is not affected and in young children even then, the recognition of this fact is very difficult. It becomes necessary with streptococcus sore throat always to bear in mind the possibility of extension to the

ear, and also that an abscess may develop under given circumstances without an examination of the tympanum revealing the presence of pus in young children. When the sensorium is not affected, then the symptoms of middle-ear trouble are the same as they are under ordinary circumstances.

The dangers of middle-ear trouble, while greatly exaggerated by the specialists, are nevertheless real. They may come in two ways: first, as a result of direct extension of the process to the brain and the meninges, and the production of thrombosis of large vessels, but principally—and this is a matter that has been largely overlooked by practitioners—by the production of cryptogenic septicæmia. As the result of the working out of this subject, undoubtedly many more cases of unpleasant sequelæ from middle-ear suppuration will be found than we have heretofore had any idea of. This, of course, opens a vista by way of production of serious symptoms in all the important organs, either in the form of sepsis, septicopyæmia, or pyæmia itself, a further description of which would be out of place in this article. A few cases have been reported in which ulceration of large vessels and fatal hemorrhage have taken place. Baader reports a case of a three-year-old boy, who had otitis media purulenta. On the twelfth day of the disease hemorrhage took place from the ear, which became severe and, not being controlled, ended fatally on the third day. The post-mortem examination disclosed a perforation of the posterior wall of the tympanic cavity and an erosion of the transverse sinus. Hessler also reports a case of ulceration of the carotid and as a result fatal hemorrhage.

Hynes reports fatal hemorrhage of the ears in a four-year old child, which occurred without premonition, the child having been left as perfectly well by the physician a short time before he was called back, to find an arterial hemorrhage from the right ear. This was apparently stopped, but the child began to vomit blood in large quantities and soon died. It was supposed that the internal carotid was torn, the blood pouring into the stomach through the Eustachian tube.

Burkhardt-Merian says that "of one thousand patients with ear trouble in forty-three to fifty-five this is the result of scarlatina." Baader states that in fifty-one cases of scarlet fever, twenty-five per cent. had ear trouble. The severe forms are the direct result of diphtheria of the pharynx. In the milder form it is a long-continued congestion of the pharynx which produces the same effect in the middle ear. In scarlatina with diphtheria, when the fever disappears, a fever associated with pains in the ears and enlargement of the lymphatics (cervical and submaxillary) develops; it is usually not a simple middle-ear catarrh but a diphtheria of the middle ear, fre-

quently destroying the drum membrane, producing great danger to hearing, even to life (meningitis, erosions of the carotid or the transverse sinus). This form of trouble usually begins during desquamation, with fever, pain in the ear, deafness, sometimes well-marked sopor. The glands are enlarged and the mastoid process is painful on pressure. After perforation of the membrana tympani the pain disappears. Of eighty-five cases of disease of the ear after scarlatina, in eighteen it was in both ears, and three of the patients were deaf-mutes. Vivy reports an epidemic in 1880 at Aumale (Algiers). Of eleven cases of otorrhœa, four developed after complete disappearance of the exanthem and the angina; seven after the disappearance of the eruption, the angina, and the desquamation. He considers the ear trouble as one of the localizations of the scarlatinal poison.

Angina gangrœnosa.—This form of angina is a very rare complication, possibly rarer at the present time on account of the care that is given to the mouth and the throat in scarlatinous patients, than it was formerly. As a rule it ends fatally. It occurs principally in hospital practice, is almost unknown in private practice, and presents a lamentable picture when it does occur. As the name implies, the principal symptom is that of gangrene. The first thing that strikes one in examining the patient with gangrenous angina is the extremely offensive odor, although it must be confessed that this is not absolutely characteristic. There is a large amount of corroding secretion coming from the mouth, and from the nose; inspection of the throat shows gangrenous patches upon the tonsil, upon the soft palate, and upon the pharynx, rarely farther forward in the mouth. These gangrenous patches are of a grayish-black color, and are depressed below the level of the rest of the mucous membrane, which is swollen around them. Very quickly these separate patches extend and melt together. Frequently the process becomes so active that perforation of the soft palate takes place in a very short time, resembling in this respect the destruction in noma. The lymphatics at the angle of the jaw, the cervical lymphatics, the submaxillary lymphatics, are very much enlarged. The general symptoms are those of great debility. The pulse becomes small, frequently slow, the temperature may be subnormal, at other times it is very high. The patient has cold extremities and his vital powers seem very much depressed.

The Lymphatic Glands.

We recognize two forms of lymphatic complication: a primary and a secondary. As has been shown in connection with the symptomatology, primary enlargement of lymphatics is common to all

cases of scarlatina. We are, therefore, justified in drawing the conclusion that this enlargement is due to the action of the scarlatinous virus itself.

In the secondary form, on the other hand, the enlargement is always due to some complication. This complication is to be found in the presence of pus-producers. So that under all circumstances enlargement of the lymphatics is to be looked upon as a manifestation of absorption either of lower forms of life or of their toxins. Various pus-producers have been found time and again in the pus coming from abscesses of these glands by various authorities, so that at the present time the etiology of these enlargements may be looked upon as successfully and thoroughly established. These enlargements are found most commonly in the glands at the angle of the jaw, the submaxillary glands, and the cervical glands, for the simple reason that the primary process is most commonly found in the nose, in the pharynx, upon the tonsils, and in the mouth. Other glands sometimes form abscesses, but this is certainly exceptional, and depends upon a secondary infection through some erosion of the skin due to processes either connected with scarlet fever or independent of it.

The mild cases usually begin from the second to the fourth week, are always characterized by a recrudescence of fever, the temperature not going very high, very commonly associated with albuminuria, and always causing an increased reduction of hæmoglobin in the blood. So that, although this manifestation may seem a very mild one, as it is locally, the general effects are very pronounced upon the patient. Examination reveals at the angle of the jaw a round, hard, glandular mass, thoroughly movable and more or less painful. From this gland can be followed up the chain of lymphatics connected with it towards the clavicle, the gland nearest the original enlarged gland being after it largest, then the one below this one, smaller, and so on until the clavicle is reached, where the smallest one will be found, showing that the infection has come from above. This induration may last, if no further development takes place, from a week to ten days. Gradually the elevation of temperature disappears, in very mild cases not even one week being necessary to produce the change; the swelling becomes less, first of the glands below, then of the original gland; painfulness disappears; the patient's general condition improves, the appetite becomes normal, the quantity of urine increases, the latter becomes clearer, albumin may or may not persist, depending upon the presence or absence of nephritis, and the gland gradually returns to its normal condition. Very frequently, however, although the local symptoms may disappear for one or two days, we are disappointed in that they again appear. After this we

must thoroughly make up our minds that instead of resolution, suppuration will now take place in this gland. There develops a mild type of septic fever, the temperature is nearly normal in the morning, but rises to 101°-102° or sometimes even higher in the evening. With this there is always more or less sweating. The patient becomes affected generally even more markedly than in the form described before. The local symptoms are better developed and we now expect to find pus in the gland. As a rule the pus forms in the more central portion of the gland first, and it takes weeks for it to appear near the surface, that is, for the abscess to point. By this time the symptoms described above, in connection with the first form, continue, and this local condition becomes a very serious complication, as far as convalescence is concerned. Under most circumstances, especially when judiciously treated, this form of glandular trouble has a favorable termination. Although secondary septic processes, especially in the joints and in the heart, may occur, so long as the infection is confined within the capsule of the gland this prognosis holds good.

Severe Form.—As soon, however, as the cellular tissue around the gland becomes infected, then we are dealing with one of the most dangerous complications of scarlet fever (cellulitis, angina Ludovici). Now the whole clinical picture is changed. We have all the symptoms of intense sepsis, the characteristic pus-producer curve, irregularly high temperatures followed by violent sweating, which are most characteristic for the inception of this condition. Albuminuria and toxic nephritis are very common. Locally we have more or less intense degrees of swelling accompanied by tension, redness of the skin, rapid production of pus; as with all of these processes in scarlet fever, whether they be upon the surface or upon mucous membrane, we have rapid necrosis going on. As the result of the swelling we have compression of parts, so that it becomes sometimes difficult for the patient to breathe (compression of the larynx). As the result, furthermore, of this œdema we have developed the much-dreaded complication of œdema of the larynx. The abscesses that are formed may be evacuated or there may be much burrowing of pus, producing on the one hand pleuritis and empyema, on the other disturbances in the cellular tissue about the larynx and about the œsophagus. The most dreaded complication is erosion of large blood-vessels followed by fatal hemorrhage. While cases are not very frequent the termination is always the same, namely, death. Baader reports, besides the one case referred to above, two cases of acute hemorrhage in scarlet fever. One was in a four-year-old boy, who had a suppurating gland in the neck which had been opened. A secondary swelling had to be opened on account of the danger from suffocation. From this there

were removed some coagula, and this was followed by a large arterial hemorrhage, which was stopped by compression. After three days a fatal hemorrhage from the nose and mouth took place. Post-mortem examination showed an opening of the carotid as a result of the suppurating process. The second case occurred in a six-year old boy who had a cellulitis of the neck which was opened above the clavicle. A week later there developed double pneumonia, profuse hemorrhage took place from the external jugular vein, and death occurred within twenty-four hours. Henoch reports two cases of fatal hemorrhage after opening a suppurating gland, and Evans three cases of fatal hemorrhage from cellulitis in the neck.

Nephritis.

The presence of nephritis varies very much in different epidemics. Very high percentages of frequency have been reported, as high as ninety per cent. On the other hand, we have statements in which epidemics have occurred without the production of any cases of nephritis.

Etiology.

The author cannot agree with Steiner, who claims that nephritis belongs as much to scarlatina as the exanthem; nor with Stephenson, who made thirty-five thousand examinations of the urine in one hundred and eighty patients and found albumin in sixty per cent. The latter believes with Steiner. that there is a scarlatinal nephritis—in other words, that there is a nephritis produced by the scarlatinal poison. The arguments in favor of this view are to be found partly in looking over the reports upon pathological anatomy and partly from other sources. If we review the reports made by the pathologists, it will be seen that in the majority of instances we have present a glomerulonephritis. While the stand that is taken that there is no characteristic form of kidney lesion for cases of scarlet fever is perfectly correct, it must be granted under all circumstances that in scarlet fever the glomerulonephritis is that form which is found most commonly. We know from experimental pathology that there are very many poisons that produce glomerulonephritis. It is more than likely that the poison of scarlet fever is to be added to this list. If cantharidin be injected into the circulation in one of the lower animals, it is almost certain that a glomerulonephritis will be produced. Possibly the association of another poison with cantharidin may cause other forms as well, but under all circumstances the glomerulonephritis is considered as characteristic of cantharidin

poisoning. Why should this not be the case in scarlatina also? As the result of clinical experience, a positive answer must always be given to the question whether there is such a thing as a scarlatinal nephritis. It is true that nephritis occurs very frequently in connection with the acute infectious diseases, especially in connection with those forms of disease in which there is a possibility of secondary infection; but if the symptoms of scarlatinal nephritis be taken into consideration, it will be seen that notwithstanding the existence of nephritis in other forms of disease, there are certain characteristics, especially the frequency of anasarca, the inception of the disease, the course of the disease, its favorable prognosis in the majority of instances, that permit the clinician to establish this form as one *per se* just as the clinician speaks of a postdiphtheritic paralysis, although neuritis occurs frequently in connection with other diseases. Another argument that can be adduced is the fact that nephritis is so very commonly associated with scarlatina. There is no other disease that has so frequent an accompaniment of nephritis as scarlatina. It is at least rational to conclude that something which acts as the cause of scarlatina eventually acts upon the kidneys. Excluding those forms of nephritis which occur in all acute infectious diseases, and including those rare cases in which the symptomatology of the nephritis is the same as that of a scarlatinal nephritis, we are justified in concluding that scarlatinal nephritis is an entity by itself. On the other hand, nephritis in scarlet fever is produced by other toxins and bacteria. A case of pure scarlatinal nephritis practically does not exist any more than an absolutely uncomplicated case of parenchymatous or interstitial nephritis. We usually find with the glomerulonephritis more or less involvement of the other parts of the uriniferous tubules or even of the interstitial substance, and sometimes, indeed, the interstitial nephritis predominates over the glomerulonephritis.

Predisposition.—For the individual case the statement can be made that whether the patient has a mild or a severe attack of scarlet fever, it is impossible to predict whether or no he is going to have nephritis. Upon the whole, however, the statement can be made that the chances are greater of nephritis following a severe attack of scarlatina than a mild one. This is especially true and admitted on all hands, if we take into consideration those cases in which there is any septic involvement. But even if we disregard these, especially if the postulate we have offered before is correct, severer cases must be followed by nephritis with greater frequency than mild ones. The question of "catching cold" has always been one that has affected our views largely as to the predisposing effects upon nephritis. With the

dawn of more exact etiological knowledge, the number believing in the effect of "catching cold" is rapidly diminishing, but even before this excellent clinicians like Hebra, Henoch, Bartels, have expressed doubts or even more as to the connection between "catching cold" and nephritis. It is a pleasure to see that Jürgensen may be added to this list. Even certain English observers are found who are willing to admit that there is no connection between "catching cold" and the nephritis of scarlet fever. While this subject can hardly be decided definitively by discussion or even by statistics, it is but fair to ask that the negative side of the question receive as much consideration as the affirmative. From pathological reasons it is impossible to conceive of "catching cold" producing an inflammation. Those who have been neglectful of this as an etiological factor claim that their results have not differed, as far as the frequency of nephritis is concerned, from the results of those who have surrounded their patients with all the precautions necessary to prevent the intrusion of draughts of air.

The individual predisposition may be general or local. There is no doubt that in certain families there is a general predisposition to the production of diseases of the kidney, as the result possibly of lack of elimination in other organs as the skin, lungs, and gastrointestinal tract. Relative insufficiency of the kidneys may exist in this disease as it does in others. That there is a local predisposition to the production of nephritis is undoubted. The kidney may be looked upon in some instances as a *locus minoris resistentiæ*. In such cases naturally inflammation takes place more readily than when the kidney is perfectly normal. For reasons not to be explained in the present condition of science, one individual will, with an acute infectious disease, have disease of the kidneys, another cerebral trouble, a third endocarditis; whether the cause is to be found in structural or functional peculiarities or in other conditions remains to be determined.

Age.—Hetzka has shown, as the result of investigations in the Elizabeth Hospital of St. Petersburg, that age seems to be a factor that must be taken into consideration. Of 138 patients there were:

Under one year	25	cases,	1	case	nephritis,	4	per cent.
Between one and two years	107	"	5	cases	"	4.6	"
Between two and three years	106	"	12	"	"	11.3	"
Between three and four years	79	"	16	"	"	20.2	"
Between four and five years	86	"	20	"	"	23.2	"
Between five and six years	82	"	18	"	"	21.9	"
After six years	360	"	60	"	"	16.6	"

It will be seen from these statistics that children under two years of age are almost immune.

The Character of the Epidemic.—Scarlet fever complicated by other infections is more apt to produce nephritis than uncomplicated forms. The intensity of the scarlatinal poison plus streptococcus infection produces the greatest number of cases that come under our observation. Vogl in one epidemic reports as high as thirty-four per cent.

Symptoms.

This complication begins most commonly at the middle or end of the second week, sometimes as late as the ninth week. The authors vary very much as to statements concerning the time of beginning. Hetzka in examining a number of cases found that in one case nephritis developed during the exanthem, in one case on the fourth day, twice on the seventh day, three times on the eighth day, three times on the ninth day, three times on the tenth day, twice on the fourteenth day. Thompson makes the statement that it develops most commonly in the second, third, or sixth week. Jaccoud believes that it begins from the tenth to the fifteenth day; Jürgensen that the most common time for beginning is in the third week. Under all circumstances, in order to be on the safe side, it is the duty of the practitioner to examine the urine every day, at least from the beginning of the second week until the termination of the third week. This can be readily done by means of the tests to be made at the house of the patient. When this precaution is taken, it will be seen that the beginning of nephritis comes much more frequently in the second week, and very insidiously, than at any other time or in any other way. Much will be spared the practitioner if this examination is made every day. Possibly much good can be done. This, however, for further discussion in connection with the treatment.

The Urine.—Before discussing the pathological urine of scarlet fever, it is necessary to say a few words regarding the normal condition of the urine in scarlatina. Albuminuria does not by any means signify a disease of the kidneys. It is true that it may be difficult under certain circumstances to differentiate between a simple febrile albuminuria and the severe forms of albuminuria that occur within the range of the normal in scarlet fever. Albuminuria that occurs during the exanthem frequently gives us no insight into the condition of the kidney, sometimes a fatal nephritis being found post mortem which did not give any evidences in the urine. At all events the febrile albuminuria, which occurs from the second to the sixth day and lasts from three to five days, as a rule means nothing more than possibly a so-called catarrhal nephritis and in the vast majority of instances disappears of its own accord without any further developments. That which can be said of febrile albuminuria in other dis-

eases can be said of the febrile albuminuria of scarlatina. Sometimes genuine nephritis develops after it, but in the experience of the author there has always been a period, varying in duration, when the urine has appeared perfectly normal before actual nephritis has developed. In the condition of febrile albuminuria the urine contains mucus and cylindroids, rarely epithelial, hyaline, or bloody casts.

A word must be said here in regard to the tests for albumin that are referred to when we speak of albuminuria. For clinical purposes the heat test and the nitric acid test suffice if used in the proper way. The heat test is to be applied by filling the test-tube three-fourths full and then boiling the top layer of the urine without heating the urine below this. In this way comparison is afforded between the urine that has been boiled and the urine that has remained cool. The only possible error that can slip in with this test is in cases of excess of phosphates. This is controlled by pouring chemically pure nitric acid under the urine with the result that where the nitric acid and the urine meet, the white ring produced by the coagulated albumin is formed. The advantage of the latter test is that it gives one an insight into the quantity of albumin and at the same time an idea of the presence of urates, which form a triangular cone some distance above the junction of the acid with the urine, the base of the cone being deeper in color, the shading gradually becoming less marked as we approach its top. All the clinical results to be referred to have one or both of these tests as their basis. If we use finer tests, albuminuria will be made even more common than it is at the present time, and again there will be no standard to compare results by. These tests are sufficiently fine to detect quantities of albumin that need be appreciated.

Peptonuria and Propeptonuria.—It was thought at one time that in finding peptone and propeptone and possibly albumoses we had a test in the urine which might give reasonable help in the diagnosis of scarlatina. Senator, in 1874, found peptone in all urine of scarlatina containing albumin. In 1876 Petri, going over this work with different tests, came to conclusions entirely different, in that he did not find peptonuria. Pacanowski, in 1885, found peptonuria before or during defervescence. Paul Binet found peptonuria in one case out of forty-three cases of scarlatinal nephritis. Arslan Ervant (1893) makes the statements that no peptonuria occurs in normal cases of scarlatina, that it always occurs in complications, that it is prognostically bad, and that it is not simultaneous with albuminuria but with indicanuria.

Sior (1874) and Schulter, using Kuhne's method (quoted by Sior), could not find peptones in scarlatina under any circumstances; so

that it seems here again one of the pathognomonic signs has disappeared with the usual constancy.

Diazo Reaction.—With the discovery of this reaction by Ehrlich, it was hoped that some result might be obtained in scarlatina if only a negative one. Ehrlich in 1882 first makes the statement that sometimes the reaction occurs in scarlet fever and sometimes not. Brewing states that he found it three times in six cases, strongest at the beginning of the eruption, disappearing during desquamation. The last author to have examined into it was Niessen, who found it in eleven cases out of twenty-three. The test then is absolutely without value so far as scarlatina is concerned.

In examining the urine it will be noticed that there are certain changes that precede the development of albuminuria. In a certain number of cases we find polyuria; in others, possibly more numerous, the quantity of urine gradually diminishes, and in making the test with nitric acid it will be found that the urates are present in excessive amount; indeed, so large is the quantity that frequently the heat test will have to be used to control the nitric-acid test, doubt remaining after the nitric test as to the existence of albuminuria. There is a constant diminution from this point on (we are now speaking only of true scarlatinal nephritis) in quantity of urine, with a corresponding increase in the quantity of albumin as soon as the albumin begins to appear. With the albuminuria we find microscopically red corpuscles, hyaline, epithelial, fatty, and blood casts. The color after a certain length of time becomes of the characteristic smoky tint, due to the existence of altered hæmoglobin. The quantity may be reduced absolutely to nothing, the longest period of anuria observed by the writer being twenty-four hours, although Juhel-Renoy reports a case of anuria lasting six days, beginning in the period of invasion, death occurring on the fifth day of the disease, 10 gm. of urine only being passed throughout the whole illness. If recovery takes place, the changes in the characteristics of the urine follow in the inverse order of those described during its development. The reaction of the urine always remains acid; its specific gravity depends upon the quantity—high with small quantity, low with large quantity—varying from 1.004 to 1.040. The quantity of urea varies with both the specific gravity and the quantity of urine. As a rule the urates are increased; sometimes uric acid is found. Usually before the albuminuria appears we have a rise in temperature. This fever continues, may last through the whole period of marked albuminuria, and may at times become quite high, especially with the development of uræmic symptoms. As a rule, however, the range of temperature is quite low. With the increase in the urates and the

increase of temperature, as a rule we are justified in prophesying nephritis, when both occur in the beginning or the middle of the second week of the disease. We are justified, furthermore, as a rule, in foretelling the symptoms that may occur as a result of this complication, and in this way raising our own authority and at the same time the confidence of our patients. The local symptoms are a tendency to abnormally frequent micturition; this is especially the case in the preälbuminuric stage when characterized by polyuria. When this symptom is well developed, there is a condition approaching to tenesmus of the bladder. Evacuation of the bladder becomes necessary during the day and during the night. This symptom, of course, disappears as soon as the quantity of urine becomes materially reduced. Pain in the back is referred to by all the authors as one of the prominent local symptoms of nephritis. The author has failed to elicit it as a symptom in the majority of patients, as the result of either subjective or objective examination.

After the appearance of albuminuria we have that of *œdema*. This as a rule begins about the eyes and the ankles, in some instances, however, in other places. The peculiarity of the scarlatinal œdema is that it rapidly becomes anasarca; the legs and then the skin of the abdomen are affected; very commonly we have ascites, and the pleural cavity and the pericardial cavity are filled up; œdema of the lungs, œdema of the glottis, œdema of the brain take place. In no form of nephritis that the author is acquainted with is the anasarca so rapidly, so universally, and so enormously developed as is the case in scarlatinal nephritis. An explanation has been offered for this peculiarity, which is accepted upon all hands, namely, that it is due not only to a nephritis, but also to the action of the poison of scarlatina upon the skin. Leichtenstern believes that the irritation of the scarlatinal poison takes place in the lymphatic vessels. Cohnheim believes that it is due, in common with other forms of dropsy of the skin, to changes in the blood-vessels. The fact remains, as stated above, that this condition is almost characteristic of scarlatina. When the urine of the patient has not been examined from day to day, the physician and with him the patients will be surprised in many instances to find this symptom developing, and to this fact is due the great number of cases that have been reported as having acquired dropsy as the result of "catching cold," when as a matter of fact the cause that produces the dropsy has been operative for a week or more before the patient has had a chance to "catch cold." Varieties of true scarlatinal nephritis are found. We have first, abortive attacks, which manifest themselves by symptoms forming a clinical picture up to a certain point, possibly without dropsy, and then grad-

ually disappearing. Next, mention must be made of the absence of albuminuria, with or without anasarca. In rare instances we find that nephritis may produce anasarca without albuminuria. Again, we may find that nephritis may be present without producing any evidences whatsoever, just as we find ordinary forms of Bright's disease without albuminuria and without certain other lesions characteristic of Bright's disease.

Mixed Cases of Nephritis.

These occur either early or late in the disease. The hemorrhagic form of nephritis may be fatal in the first seventy-two hours. The only evidences that we may have in these cases are the presence of albuminuria and the great diminution in the quantity of urine. So far as the existence of hæmaturia is concerned, this may be found in the non-hemorrhagic form and may be absent in the hemorrhagic form. So that in individual cases, no conclusion can be reached from uranalysis as to the nature of the changes going on in the kidneys. In the cases occurring later, after the eruption has appeared or even later than this, there is the greatest variety in the symptoms. Usually this form follows a sore throat and develops very suddenly. In a few hours the urine, which has been perfectly free, contains albumin, becomes blood red, and is diminished in quantity. The anuria is frequently followed by polyuria with or without hæmaturia. In the latter instance the course is more favorable, although sometimes marked dropsy or even uræmia develops notwithstanding polyuria. In three cases (Leichtenstern) a uræmic attack was the first sign of nephritis, the urine having been examined three or four hours before and found free from albumin. In two cases dropsy set in from twenty-four to forty-eight hours before albumin appeared in the urine, and afterwards hæmaturia and oliguria appeared. On the other hand, hemorrhagic nephritis occurs with anuria and without dropsy.

Uræmia.

Usually uræmia develops with distinct prodromal symptoms. These consist in disturbances on the part of the gastrointestinal tract and disturbances on the part of the nervous system, fever with increased pulse rate, and finally the changes in the urine, consisting often in anuria, or, when the urine is passed frequently, it is small in quantity and comparatively low in specific gravity, indicating that the secretory function of the kidney is very much disturbed. The symptoms on the part of the gastrointestinal tract most commonly are vomiting and next to this diarrhœa. The temperature begins to

rise, very little possibly beyond that of the day before, but in a short time, twenty-four hours usually, it goes up to an appreciable height. If the suppression of the urine and the intoxication are great, the temperature may go very high—106°–107°. This, however, happens only in very bad cases. On the part of the nervous system, the symptoms can probably be considered as most important and, as it were, those that dominate the picture of uræmia. As has been shown before in connection with the etiology, Leichtenstern has attempted to classify the symptoms of uræmia and to refer them to œdema and possibly inflammatory changes in the various parts of the brain. It is not definitely settled that this etiological view is absolutely correct. Certainly, so far as the gastrointestinal symptoms are concerned, the probabilities are that we are here dealing with an eliminative process just as much as we are in the skin dealing with an eliminative process when sweating, which is an almost constant symptom of uræmia, takes place. But however this may be, whether the intoxication produces disturbances in the nervous system by direct irritation, or whether there is elimination into various parts, gastrointestinal tract, uterine tract, respiratory tract, the skin possibly, as has been referred to above, the endothelial cells of the blood-vessels and those lining the lymphatics, the fact remains that the principal symptoms of uræmia are manifested on the part of the nervous system. We have in the beginning, as has been indicated, only the mildest symptoms, and in some instances the affection does not go beyond the development that has been outlined; in other words, we simply have vomiting and diarrhœa, possibly tinnitus aurium, headache, slight elevation of the pulse and temperature with the conditions mentioned in the urine. The next symptom that develops and which causes anxiety is the beginning of convulsive movements. With this are associated more or less sopor, stupor, and finally uræmic coma. The convulsions are of more or less intensity, varying from the slight twitching of the eyelids and corners of the mouth to the very well-developed epileptoid tonicoclonic uræmic convulsion. Usually in mild cases the convulsions are confined to one or more groups of muscles, sometimes one-sided, sometimes both-sided; at other times they become general. When the convulsions are confined to one group of muscles, the condition of the mind is not that of complete coma. When, however, the convulsions, as happens in well-marked cases, develop as true uræmic general convulsions, then the patient is comatose, at least for a given length of time, after each convulsion. The author has had occasion on more than one instance to study the condition of the mind between the convulsions, and while the patient, if old enough, seemed to regain consciousness and speak

apparently rationally, yet when his attention was called to the conversation after recovery had taken place, everything that had occurred during this time of apparent consciousness was absolutely blank. These convulsions may last a very short time, only a few minutes, or thirty or forty minutes or longer. At times they are repeated at short intervals; at other times the intervals are longer. With this condition of uræmia there may develop peculiar conditions of the nervous system, amaurosis, aphasia, hemiplegia, to be referred to more in detail further on. The amaurosis usually lasts only during the period of convulsion—sopor or coma; in the interval between the convulsions when the patient is normal it disappears. Frequently amaurosis extends over weeks, always, however, ending in recovery. Aphasia and hemiplegia, frequently going together, also last during the uræmic state and then disappear. During the convulsions or during the stage of coma with convulsions, death may take place, the result of many causes, notably œdema of the brain, hemorrhages into the brain, or œdema of the lungs.

Prognosis.

Returning now to the general subject of nephritis for a moment, it can be said that the prognosis is good as far as recovery is concerned; recovery in every way, both as to life and as to *restitutio ad integrum*, although a few cases are on record (Litten, Leyden) in which chronic nephritis has followed scarlatinal nephritis. The author has seen one instance of this in a child six years of age which ended fatally after a duration of nearly six months after an attack of scarlet fever.

As recovery takes place in the vast majority of instances, the convulsions become less marked, the intervals become longer, consciousness gradually reappears, the nervous symptoms referred to above disappear; in a comparatively short time the nervous condition at least is returned to its normal, although the resistance of the nervous system is diminished for a greater length of time. With the disappearance of the uræmic condition, the nephritis runs its accustomed course, getting well in six weeks to two months from the first appearance of the albumin. This description holds good for the ordinary forms of scarlatinal nephritis. In the grave mixed cases the picture of uræmia is an altogether different one in that it is more foudroyant. These cases have already been referred to and not much further need be stated. They may develop with or without anuria; they may develop on the basis of a perfectly normal urine; they may develop so suddenly that it is absolutely a matter of surprise, and as quickly as they develop so suddenly do they become fatal. This form of trouble can be looked for only when there is somewhere in the body

a primary depot of pus-producer deposits which may give rise to this combination of symptoms, or when, as it frequently happens, there is present nephritis with the ordinary evidences and in addition to this there develops a pus-producer depot. On the other hand, we may find nephritis due to pus-producers in scarlatina, which may run its course in the mildest way; lasting a much shorter time than indicated above, and producing few constitutional symptoms. It is more than probable that the febrile albuminuria, referred to above, is the indication of a mild form of pus-producer nephritis. Indeed the worst forms of mixed nephritis are found in the first week of the disease, while pure scarlatinal nephritis develops later.

The Heart.

That which is true of nephritis of adults in other conditions is true of nephritis in scarlatina, namely, that the heart is always enlarged. Most frequently the enlargement is left-sided, sometimes both (see the section on Pathology). This has been overlooked for the simple cause that it has been rarely looked for. Ordinary percussion of the heart will show that in every case of scarlatinal nephritis the heart is dilated at least during the maximum intensity of the trouble. This is not to be wondered at when we take into consideration the enormous possibility of dilatation that exists especially in the heart of the very young. As a rule in these cases insufficiency of one side of the heart is not produced, but when the dilatation becomes very great then the left side becomes functionally insufficient and with this there develops dilatation upon the right side of the heart. The symptoms that develop are those that we see under ordinary circumstances of dilatation of the heart. Thus we may have tachycardia, tachypnœa. With this there is diminished tension in the arteries; the pulse as a rule is very rapid but sometimes may be very slow, due to uræmic complications. Tachypnœa as a rule occurs without any symptoms on the part of the lungs; tachycardia without the presence of anything more than simply the dilatation of the heart. Auscultation in these cases may or may not reveal a bruit. Great care must be taken not to consider these bruits due to endocarditis. They are as a rule the result of relative insufficiency, and after the dilatation has disappeared these bruits disappear as well. Recovery from this heart lesion takes place in one of two ways. If the condition lasts a sufficient length of time, compensatory hypertrophy is likely to follow. If, on the other hand, the condition producing this trouble lasts only a short time, then the dilatation disappears without any change in the myocardium. With acute dilatation of the heart there

is frequently found enlargement of the liver. When this enlargement develops suddenly and is very marked it must be looked upon as an exceedingly grave omen. The author has seen the liver extend to the umbilicus within twenty-four hours in these cases. The ordinary enlargement found in dilatation of the right side of the heart need not cause any uneasiness, as it disappears when the cause is removed.

The other forms of cardiac trouble are either septic or rheumatic. Ashby states that in nine hundred cases of scarlatina he has seen synovitis twenty times; of these one each had pericarditis and pleuro-pericarditis, none endocarditis. On the other hand, endocarditis was not uncommon with rheumatoid affections which developed at the end of the third or beginning of the fourth week. Nephritis he considers a common cause of heart disease. In one hundred or more post-mortems he never saw endo- or pericarditis without nephritis. In most cases the myocardium was pale and flabby, and the endocardium upon the papillary muscle was cloudy. Ashby has never seen a hard or leathery myocardium after scarlatina. He considers it probable that in most cases of nephritis dilatation of the left heart occurs, which can be demonstrated for one week. In pyæmia, which is almost always fatal, endo- and pericarditis are common. It is not necessary to dilate on the symptoms of these latter forms as they are the same whether developed upon the basis of scarlatina, on ordinary septicæmia, rheumatism, or what not. From a clinical point of view we would be inclined to the statement that valve lesions are more common as the result of scarlatina than is indicated by the estimate made by Ashby. It is always well to watch the heart in any case of scarlatina.

Scarlatinal Rheumatism.

Much has been grouped under this heading, from the slightest pain, with or without swelling in the joints, to the most intense pyæmic manifestations. Both Bokai and Ashby admit that tuberculous abscesses may occur in scarlatina and have been called scarlatinal rheumatism. The frequency of the affection of the joints has been estimated by Vogl in two epidemics, 1884–85 and 1894–95, in the former 13.6 per cent., and in the latter 10.6 per cent.

Certainly, so far as the author's observation goes, this is a liberal estimate. Of the twenty cases of synovitis referred to above in the nine hundred cases of scarlatina, Ashby says there can be distinguished the following forms of joint affection: First, synovitis; second, pyæmic synovitis; third, acute or subacute rheumatism; fourth, scrofulous joint affections. All these cases of synovitis were severe, two dying and all characterized by the fevers being un-

usually prolonged as the result of necrotic ulcers of the tonsils and soft palate. Most commonly the wrist and finger-joints were affected. Sometimes there occurred inflammation of tendon sheaths. Over the affected parts the skin was rarely reddened. These complications usually developed towards the end of the first week. They disappeared in a few days without any local relapses. Cardiac bruits were frequently heard, but they lasted only a short time. It is doubtful whether the salicylates did any good. In the second form only three cases were observed, two of which died. In the third form, relapses of former attacks of inflammatory rheumatism were common during scarlet fever and could then cause endocarditis. The fourth form could, even if apparently perfectly cured, again break out, suppurate, and cause pyæmia. Bokai distinguishes two kinds, serous and purulent, the former usually benign, acute or subacute, or developed into a chronic form, tumor albus. Exceptionally a serous synovitis became purulent. The serous form became dangerous only when inflammation of the serous cavities took place. It could be distinguished from acute articular rheumatism by its mild course, spontaneous restoration, absence of relapses, the affection of fewer joints, and prompt benefits from salicylates. It developed as early as the third day of the eruption, at other times very much later. The purulent form is a part of general septicopyæmia, extremely unfavorable in prognosis.

If we read this statement by the light of modern investigation, we must come to the conclusion that all joint affections of scarlet fever are either septic, rheumatic, or tuberculous. The septic can be subdivided into the mild and grave forms (pyæmic) and always presuppose, as indicated by Ashby, a primary septic lesion somewhere. Scarlatina predisposes to ordinary rheumatism. Whether this is due to the fact that rheumatism itself is the result of invasion of pus-producers, as is claimed by the French school, or not, it is impossible to state.

The symptoms have been described in the excerpts given above.

The *prognosis* in every case of scarlatinal joint affection is not good in the septic forms, because it indicates a generalization of the septic infection; in the pyæmic form, because it means an additional intensity of infection and in this way leads to death. Even if the patient recovers, so many ankylosed joints may be left that his condition is a very pitiable one. The author has seen one instance in which both hip-joints, both wrist-joints, both elbow-joints were left almost completely ankylosed; the shoulder-joints, knee-joints, and ankle-joints not completely; when the patient grew up to manhood (the attack having occurred when he was but five years of

age), the hip-joints remained practically permanently ankylosed, the other joints, as the result of constant exercise, being loosened up somewhat.

In rheumatic arthroses of scarlatina the prognosis *quoad vitam* need not be very bad, but in a large percentage of cases endocarditis follows and with it a damaged heart.

Purpura Hæmorrhagica.

One of the rare complications of scarlatina is purpura hæmorrhagica. We can distinguish two forms: one a mild form, the second that form that has been called fulminating or foudroyant. The mild form of scarlatinal purpura hæmorrhagica is not to be distinguished from this disease as it is seen anywhere else. The foudroyant form develops suddenly about the second or third week of the disease, not uncommonly with albuminuria or possibly when the patient is enjoying comparatively good health. It is difficult to state what the cause of this form of disease may be, but it has seemed to me that its etiology is the same as that of the other hemorrhagic forms of the disease found in children. The two cases that I have seen have developed as the result of a secondary infection following an attack of influenza. In these the purpuric manifestation in the skin showed itself in the form of large ecchymotic patches. In the one instance at the end of forty-eight hours almost the whole of the abdomen and the greater part of the lower extremities were discolored by a bluish transudation of blood-coloring matter. Upon the legs and the arms as well as upon the face were found purpuric spots. Death took place at the end of seventy-two hours in the one instance, at the end of forty-eight hours in the other, both patients having had epistaxis and both dying in coma, so that the conclusion could be arrived at that hemorrhages had taken place into the brain. In the mild cases the peculiar form of stomatitis found in this disease can be distinctly observed; in the severe ones death comes too rapidly, so that the stomatitis does not have time to develop.

The Gastrointestinal Tract.

Diarrhœa is a very common symptom in connection with scarlet fever, especially in the period of invasion and the first part of the period of eruption. As has been shown in connection with the pathological anatomy, the gastrointestinal tract takes more or less part in the manifestations as we see them upon the skin. An accurate statistical report in reference to this symptom would undoubtedly show

that diarrhœa, usually of the small-intestinal type, is present in the majority of instances in scarlet fever. Sometimes, especially in malignant cases, it does occur that enterocolitis develops, and under such circumstances it is to be looked upon as a very severe complication and a manifestation of the general sepsis. In the period of desquamation a secondary infection of the intestine may first manifest itself and then again may we have the symptoms of an extremely violent attack of enterocolitis, which is a very serious complication. In connection with nephritis, the uræmic condition, diarrhœas are not uncommon. They are to be looked upon as eliminative and, unless debilitating to the patient, of comparatively little importance. When they have a tendency to debilitate the patient or are indeed a part of his debilitated condition, then special attention must be paid to them.

The ordinary gastrointestinal disturbances due to errors of diet may be found in scarlatina as in connection with any other diseases. It must always be remembered in treating patients with scarlet fever, that the gastrointestinal tract is especially liable to disturbances.

When the metabolism of the body has been so altered by the changes in the blood due to the action of the scarlatinal poison or to secondary infections, then we will have developed that condition that is summed up under the term *cachexia*. In this condition diarrhœas are of common occurrence. They must be looked upon here as part and parcel of the whole change in metabolism, producing, as it were, a paralytic condition of the whole glandular apparatus of the gastrointestinal tract, increasing putridity, preventing digestion and absorption, and naturally producing thinner stools.

The older writers speak of a condition called "scarlatinal typhoid." At the present time this term has been discarded, and justly so. In scarlatina, as in any other disease, there may be produced a typhoid state, and the author has in mind a large and malignant epidemic that took place over twenty years ago in Cincinnati, in which a great number of patients fell into the condition that might be called a typhoid one, very alarming and in which condition not a few succumbed. In this epidemic, when the patients recovered, they did so usually after passing through a state of sopor lasting twenty-four to thirty-six hours, accompanied by a fall in temperature and a comparative fall in the pulse rate, from which the patient gradually awoke and after which all the organic functions seemed to return to the normal condition.

Complications on the Part of the Respiratory Tract.

It has been stated, and justly so, that membranous croup is a rare complication of scarlatina, but that it does occur has been emphasized by a great number of authors. Now that the one-sided view that membranous croup always means true diphtheria is being thrown aside, we are willing to recognize the streptococcus pseudomembranous form of croup, and this is notably the form that occurs in scarlatina. Bronchitis may be present as a complication, as a rule having nothing to do with the clinical picture of scarlatina, being a secondary infection imposed upon it. Except in those cases in which there is a primary deposit of pus-producers, the bronchitis runs its course benignly, as it does in children without scarlatina. On the other hand, when there is this deposit, bronchial catarrh must be looked upon as a very serious complication, and in not a few cases it leads to catarrhal pneumonia, which under these circumstances may be looked upon as a fatal complication. Bronchial catarrh, when developed upon the basis of nephritis, is always to be looked upon as an extremely grave complication. We need only refer to the condition of the heart and then it will be seen how bronchitis and pneumonia produce so grave a combination. The heart, already dilated and its myocardium weakened, now has to pump the blood against an increased resistance through the lungs. As a result that most dreaded of all complications, œdema of the lungs, develops in a comparatively short time. Pneumonias, both catarrhal and croupous, have been found in scarlatina more frequently upon the post-mortem table than *intra vitam*. The prognosis is that of the pneumonia itself or that of pneumonia developed upon a bad case of scarlatina.

Complications with Other Diseases and Diseased Conditions.

Scarlatina has been found developed upon measles, upon varicella, upon variola, upon typhoid fever, upon erysipelas, upon malaria, and upon pertussis, and the converse has been repeatedly found, that upon the basis of scarlatina these various diseases develop. In regard to a complication of scarlatina with the other acute infectious diseases, it will be well to quote the conclusions arrived at by Bez and verified by Klein, who has collected sixty-eight cases of scarlet fever and measles, fifty-one of variola and scarlet fever, and thirteen of scarlet fever and varicella. He states that the most common combination is scarlet fever with another exanthem, for the reason that the

period of incubation of scarlet fever is very short. The mortality in these cases was 22.2 per cent. As far as prognosis is concerned for the combination it is worse the later measles develops upon scarlet fever and better the later scarlet fever develops upon measles. Typhoid fever does not influence the course of scarlet fever, but the symptoms of typhoid fever disappear during the eruptive stage of scarlatina. Usually, as Murchison has noticed, typhoid fever is the first to occur.

Murchison observed ternary combinations in a number of instances. Twice scarlet fever, measles, and varicella; twice scarlatina, vaccina, and variola. He comes to the final conclusion that simultaneous eruptions do not interfere with each other as a rule, except that there is a retardation in development of vaccina and variola by scarlet fever and measles. Also, when measles and scarlatina occur together, the disease which appears first is usually shortened by the one appearing next. The latter agrees to a certain extent with the view of Fleischmann, who shows that if both exanthems develop during the period of eruption, the course of both is shortened; or, if one chooses to put it so, the second makes the first milder and in its turn is shortened in its course. This, however, is not the rule, as has been stated before, and considerable doubts have been expressed as to the general applicability of this statement.

Tuberculosis does not bear any direct relation to scarlatina. In this respect scarlatina differs most widely from measles. Barthez and Sanné, in summing up the relation of scarlet fever to tuberculosis, state, first, that tuberculous patients rarely take scarlatina and when they do the course of the disease is anomalous; secondly, patients that have recovered from tuberculosis take scarlet fever more frequently than those in the active stage of the disease; thirdly, autopsies rarely show the presence of fresh tubercles or degenerated tubercles.

The writer has not been so fortunate as these distinguished authors. In more than one instance has he seen tuberculosis develop after an attack of scarlatina. It is true, there has been no direct relation between the two and the development of tuberculosis has come only after a certain length of time had elapsed, the shortest period being five months. When the lymphatic glands remain enlarged for an unusually long time, tuberculosis should be kept in view and be guarded against. It would be strange indeed if the chronically enlarged lymphatics of scarlatina should react differently to tuberculosis than those formed as the result of other causes.

Puerperal and Surgical Scarlatina.

In these combinations scarlatina presents itself as it does under ordinary circumstances. There is nothing peculiar about scarlet fever in the puerperal state nor in surgical cases, except, first, that the puerperium and the surgical state increase the susceptibility to infection, as has been indicated before; and, secondly, as will be shown, the prognosis is very much worse when the scarlatinal poison has been introduced more or less directly into the circulation, the latter probably being the reason for the increased susceptibility. Goodhart in an epidemic of scarlatina saw twenty-five cases, of which seventeen had been operated upon. One had an abscess and seven were without external lesions. In thirteen cases antiseptic treatment had been employed, yet the patients contracted scarlatina, but, curiously enough, the wounds continued to do well during the course of the disease. Trélat, on the other hand, saw bad results upon the wounds. Paget has expressed the view that sudden deaths on the second or third day after operations may be due to undeveloped scarlatina, and Goodhart is inclined to believe in the truth of this observation. Riedinger reports nine cases developed from one to nine days after operations or wounds. Three were physicians who had been exposed repeatedly to scarlatina but were infected only after having been wounded. He thinks there is some relation between wounds and scarlatina. Browne has seen scarlatina develop in operated cases in from six and a half to sixteen hours. His observations are apparently perfectly reliable and correct. Sörensen claims that wounds, especially tracheotomy, and the puerperal state predispose to infection, the period of incubation being very short. In thirty-eight cases the eruption appeared in twenty-nine before the third day after the injury and in seven within the first twenty-four hours.

Upon the whole we may state that there is a difference between the infection of patients that have been operated upon or in the puerperal state and the ordinary cases of scarlatina. Indeed, we may say that there are two kinds of puerperal and surgical scarlatina. In the one instance it is a scarlatina developed as the result of the ordinary modes of infection, and then the course of the disease in no way differs from the course of the disease under ordinary circumstances. In the second class the infection takes place either through the puerperal endometrium or through an open wound, and then the whole picture of the disease is changed. The period of incubation is very short, the eruption may be well marked, as well as the desquamation; the prognosis is very bad, especially in puerperal cases.

Several instances are on record in which the fœtus has also become infected (Leah, Salles). The prognosis does not seem to be so bad for the child as for the mother.

Sequelæ.

We may speak of two kinds of *relapses* as occurring in scarlet fever, the one to be looked upon as a false relapse, better possibly as a recrudescence of the original process, and the second as a true relapse. The false relapse occurs usually in the neighborhood of the second week of the disease. It is characterized simply by a recrudescence of the eruption, possibly accompanied by an increase in temperature and pulse rate or by renal symptoms; all as a rule with very much less violence than occurred during the first outbreak of the disease. The true relapses, on the other hand, are characterized by the fact that the disease process has come to an end, that the patient is in convalescence, when the characteristic new attack develops with all the symptoms of the first. Trojanowsky called attention to very peculiar forms of relapsing scarlatina and measles, and while very many of these cases have been doubted and no one else has ever seen epidemics of this nature, a careful study of similar cases undoubtedly leads one to the conclusion that they were relapsing forms. The most complete collection of cases of relapses has been made by Koerner, who has drawn the conclusion from a study of thirty-nine cases that relapses occur principally between the ages of seven and fourteen, but no age is exempt. In some cases there seems to be a family predisposition. This view, however, is not accepted by others who have seen relapsing cases. Thus, May reports one case of relapsing scarlet fever in a family in which the other members were affected, but only this one case of relapse occurred. The prognosis in these cases is not worse than in the ordinary forms of scarlatina. Indeed, the patient does just as well in the second attack as he does in the first, unless the second attack be worse than the first on account of other complications.

Hardly any other disease is so much feared by the laity, so far as the sequelæ are concerned, as scarlatina, and undoubtedly in days gone by, when the treatment was even more empirical than it is at the present time and consisted principally in bad hygiene, poor food, and worse nursing, this fear was undoubtedly justifiable. At the present time, with our views regarding sepsis and asepsis, this whole question has been materially changed, and yet, with all the care and all the attention that may be given to individual cases of scarlatina, certain sequelæ do occur. We have already referred to affections of the ear. After streptococcus infection

of the nose and throat with the accompanying eye troubles, it is not an uncommon experience to find that the nose or throat and the eyes are left in conditions of chronic inflammation. The writer has seen cases in which the disturbances in the nose, in the eyes, and in the throat have remained for years. Indeed, in one instance and notwithstanding the most careful attention and local treatment, ozæna as a sequela has remained practically throughout the life of the individual. The lymphatic glands in some of these cases remain hardened and enlarged for a great length of time. The joints, especially in pyæmic conditions, may remain deformed for the life of the patient, and sometimes pitiable conditions are set up in this way. Deformities produced by cellulitis are not to be avoided. Torticollis and facial paralysis, the latter of a permanent nature, are to be considered among these. The cachexia that sometimes follows scarlatina has already been referred to and may with bad surroundings, poverty, and poor food, lead to death. Indeed, the prognosis in this condition of cachexia is always a very dubious one.

On the part of the nervous system we have, as Putnam puts it, "optic neuritis, apparently without meningitis," and the same may be true of epilepsy (Gowers). Meningitis, except from secondary infection, is rare, but does perhaps occur even in early stages (Bendel). Focal hemorrhagic encephalitis is reported (Fürbringer). Spinal affections and multiple neuritis are rare (Putnam). To these there may be added chorea, not an uncommon sequela, hysteria, and psychoses. With the advance in the study of nervous diseases it will be found that the nervous system in all probability is damaged to a greater extent than we have reason to suppose from the reported cases up to the present. Especially is this the case in those patients in whom there has been a marked streptococcus infection.

On the part of the heart, scarlatina must be looked upon as one of the diseases producing permanent heart lesions in childhood.

It has been well recognized for a long time by dentists that scarlatina has a decided effect upon the permanent teeth before they come through. It is not an uncommon experience with the writer to hear good dentists make the statement that the patient has had scarlatina at a given time simply as a result of an examination of the teeth. The changes in these are characterized by a certain amount of friability and especially a lack in enamel formation, and, upon the whole, the teeth have lost their normal resisting-power.

Furunculosis, sometimes of a very severe type, can be looked upon as one of the sequelæ of scarlatina. In rare instances desquamation has kept up for a great length of time; in one instance that came under the observation of the author the patient for years after-

wards, at certain times of the year, had erythema, the result of which was the production of more or less desquamation very similar to the desquamation of scarlatina.

Diagnosis.

While in an epidemic the diagnosis of scarlatina does not become a matter of difficulty, in individual cases sometimes one has to wait a few days before being able to make up one's mind that the diseased condition present is scarlet fever. There are many acute conditions that simulate scarlet fever, but if all the various features of the disease are taken into consideration in practice it rarely becomes a matter of difficulty to make the diagnosis.

As Hebra said of eczema, any one who knows this disease knows all of dermatology, so we may say of scarlatina, any one who knows scarlatina knows all of the exanthematous diseases and possibly a little more.

Measles.—Among the exanthematous diseases, it is especially measles and German measles in which mistaken diagnoses can occur. In regard to the latter the differential diagnosis is considered in the article on that disease in this volume. The differential diagnosis between measles and scarlatina can be readily made if one takes into consideration the nature of the epidemic. It is unlikely that scarlatina and measles are going to occur in epidemic form together, although, as has been seen, scarlatina and measles frequently develop in the same individual at the same time. The principal points of difference between the two diseases are as follows:

Measles.	Scarlet Fever.
Period of incubation lasting in the neighborhood of two weeks.	Period of incubation very short, at the longest five to seven days.
Period of invasion three times twenty-four hours.	Usually twenty-four hours.
Symptoms of the period of invasion, on the part of the respiratory tract: suffused conjunctivæ, sneezing, coughing, maximum temperature at the beginning of the period of invasion, second day lower, third day also low.	Symptoms on the part of the gastrointestinal tract: fever steadily increasing as the period of invasion continues.
Enanthem developing in the form of papules of measles, upon the anterior pillars of the fauces and soft palate. Bluish color of the mucous membrane of the mouth as well as of the tongue, becoming more marked as the period of invasion develops.	Enanthem appearing upon the soft palate and the posterior pillar of the fauces. Red, not discrete, confluent. Tongue coated as in gastric disturbances, sometimes at the end, papillæ very much injected and prominent. Pulse higher than accounted for by the temperature.

Measles.	Scarlet Fever.
Period of eruption: measles appearing upon the face.	Eruption appearing upon the chest; face free or flushed.
Maximum development in from three to four days, from above downward.	Maximum development, from five to six days.
Character of eruption: measles always of a more or less bluish tint with much swelling; discrete, circular outlines.	Well-marked scarlet color, confluent, red, with slight elevations at the openings of the glands.
Temperature: second maximum arrived at within twenty-four hours of the appearance of the eruption.	Temperature continues high until the eruption begins to fade.
Enanthem fading sooner in measles; tongue continuing with its bluish color until eruption begins to fade.	Development of the strawberry tongue.
Symptoms on the part of the respiratory tract remaining or increasing in intensity.	Symptoms on the part of the gastrointestinal tract disappearing. Symptoms on the part of the throat and tonsils increasing.
Period of desquamation: Desquamation furfuraceous, apt to be overlooked. Whole course terminated in two weeks.	Desquamation beginning furfuraceous, becoming lamellar, large scales of skin desquamated, lasting four to six weeks. Process ended at that time.

While measles is the exanthem with which scarlet fever may most easily be confounded, there are other conditions of the skin in which it sometimes is difficult to make a differential diagnosis. Foremost among these are the so-called *scarlatiniform eruptions* produced by various agencies: erythemata, drug rashes, septic eruptions, the erythema of diphtheria and of influenza. Among the drugs, which in the author's experience have produced this form of eruption more frequently than anything else, will be found quinine, although there is a great variety of drugs that do produce this rash. If here the diagnosis is held in abeyance twenty-four to forty-eight hours, as a rule no difficulty will be experienced in coming to a definite conclusion. The septic eruptions may, and not unfrequently do give rise to difficulty in diagnosis, but if the previous history be taken into consideration, as well as the non-characteristic appearance of the eruption as to its place of beginning, as to its characteristics, and as to its duration, difficulty will rarely be found in distinguishing this form of trouble. In diphtheria the rash is much more transitory, and with the bacteriological diagnosis of diphtheria, taking into consideration that true diphtheria rarely occurs in the beginning of scarlet fever, again no difficulty will be found in differentiation. Far more difficult is the form of scarlatini-

form eruption that appears with influenza. In this condition the diagnosis is sometimes impossible. While there is nothing that can be positively called an enanthem, the rash may be that of an abortive attack of scarlatina, appearing not uncommonly first upon the chest; the fever may be that of a mild attack of scarlatina. In certain epidemics symptoms on the part of the gastrointestinal tract prevail and in some cases a certain amount of, it is true precocious, desquamation has taken place. Again here we must be guided by the genius epidemicus, and by watching it will be seen that especially the enanthem does not develop as it should, the absence of the strawberry tongue being notable; it will be found, furthermore, that in the course of the first forty-eight to seventy-two hours symptoms on the part of the respiratory tract begin to develop, and especially will it be noted that patients who have already had scarlatina will be attacked just as frequently as children that have been protected.

Erysipelas is constantly being mentioned as a source of error in diagnosis. It would be an exceptional case of erysipelas which would produce the characteristic appearance of scarlatina including the place of appearance and the peculiar form of eruption with its spread. If we take into consideration, furthermore, the antecedents of a case of erysipelas, it will be seen that the chances are very largely against this error of diagnosis.

In the *newly born* the diagnosis of scarlatina becomes almost an impossibility. If we take into consideration the normal condition of the mouth and the skin in the newly born, it will be seen that it takes a certain amount of diagnostic bravery to state that a newly born infant has scarlatina. Yet such can be done exceptionally, taking into consideration the antecedents, together with the normal course of the disease when followed by desquamation at the proper time. Great care, however, should be exercised in pronouncing a case scarlatina in the newly born.

In the *colored race* the diagnosis is also extremely difficult. In the few instances that have come under the observation of the writer, the diagnosis has been made upon the nature of the enanthem as much as upon the character of the exanthem. Given a very dark-colored negro and the redness of the skin is not apparent, except in those places where the skin is unusually light colored, places fortunately where the scarlatinal eruption appears in full development, namely, the palms of the hands, the soles of the feet, and the axillæ. In a mulatto or an octaroon the difficulty of diagnosis is not so great, for the simple reason that the scarlet shade of the eruption is easily discerned.

As has been stated before, if the natural history of an attack of scarlet fever be carefully followed, it will be found rare in practice to make an error in diagnosis.

Prognosis.

The prognosis generally depends principally upon the nature of the epidemic. What has been said under the heading of morbidity and susceptibility can be referred to in this connection. The statistics in regard to the various nature of epidemics are very large and so far as the mortality is concerned, quite satisfactory. They will require revision at some early date because, after all, the number of cases occurring, that is morbidity as related to mortality, is the quantity that we wish to get when judging of the virulence of an epidemic. However, until the reports are made more fully in regard to the morbidity, we must for the present take the number of deaths as deciding this question.

The mortality varies very much in various epidemics, and it is with great comfort that the physician says to himself in any individual case that he is dealing with a mild epidemic. Hillier states that in the London Fever Hospital the mortality varied from 1 : 6 to 1 : 40; in the Children's Hospital from 1 : 3 to 1 : 11. Johannessen, who has collected 84,580 reported cases with 12,789 deaths in Norway, comes to the conclusion that in Norway the mortality is 14.17 per cent. He states that when the mortality is 13 per cent. normal conditions prevail; when it goes above, the epidemic is a severe one, when below it is mild. It must be remembered in this connection, however, that Johannessen reports that in a certain epidemic in certain parts of Norway the mortality went as high as 90 per cent. Hirsch states that the mortality may vary from 3 per cent. to 30 per cent. He and Thomas claim that the normal mortality from scarlet fever is 10 per cent.; when it is above this the epidemic is a severe one, when it is below it is mild. In private practice no such mortality as 10 per cent. is to be expected; at least this is the experience of the author.

Epidemics may begin mildly and end as malignant epidemics. As a rule the opposite holds good. Why epidemics begin mildly and end severely cannot be explained, but the fact has been observed so frequently that there now can be no doubt about its occurrence.

For the individual the prognosis depends first upon the mode of infection, secondly upon the nature of the epidemic, thirdly upon the individual himself, and fourthly, upon the nature of the compli-

cations. Before we go on to discuss the prognosis so far as the individual is concerned, the broad, general rule can be laid down that in no disease is prognosis more uncertain than in scarlatina. The physician who is careful will always state to the patient or his surroundings that it is impossible to say what the outcome of any case of scarlet fever may be. The mode of infection has already been discussed under the heading of susceptibility; the individual and his surroundings as well under the same heading. In broad general terms prognosis can be divided into two acts: first, the prodromal period and period of invasion; secondly, the period of complications. During the period of invasion and the beginning of the period of the exanthem we determine upon the gravity of the attack. The broad rule can be laid down that if violent symptoms on the part of the nervous system do not appear within the first seventy-two hours after the inception of the disease, the chances are that we are dealing with a non-malignant case of scarlatina. In detail the prognosis is bad, first when the temperature is abnormally high or abnormally low, by the latter is meant especially subnormal temperatures; when the pulse is out of relation to the increased ratio normal to scarlatina; especially, however, with the appearance of nervous symptoms that cannot be explained by the increased temperature. We may expect certain symptoms on the part of the nervous system in all normal cases of scarlatina: delirium, restlessness, pain, more or less somnolence; but stupor, coma, convulsions must always be looked upon as bad omens. The way in which the eruption appears is to be looked upon as of prognostic value. Thus, the eruption may develop and in the presence of unpleasant general symptoms disappear. By the laity this is looked upon as a driving in of the eruption; as a matter of fact the eruption of scarlatina cannot be driven in. It simply means that all the blood has gone to the internal organs or possibly that the scarlatinal poison no longer causes the proper reaction on the part of the vasomotor centres. The eruption may appear in bad cases in improper places; instead of appearing upon the chest first, it may be noticed upon the limbs or upon the back. In cases in which the eruption is badly developed, only one of two conclusions can be arrived at, namely, either the patient is suffering from a very mild abortive attack, or, on the other hand, he is suffering from an attack of extreme virulence. The hemorrhagic forms of eruption are not always the mark of a malignant attack. While it cannot be denied that hemorrhagic forms of eruption are most common in bad cases, the fact still remains that in some individuals any form of eruption that takes place upon the skin will become hemorrhagic without this meaning anything especially bad. In order to determine the nature of the

attack the character of the eruption and the place of its appearance, combined with the general symptoms, will always be sufficient.

The complications, in the second act, affect the mortality under normal circumstances more than do the malignant attacks. Among these are especially to be dreaded sepsis, which may not begin to manifest itself until the second week of the disease, although it is most commonly the cause of malignancy. The complications that affect the prognosis at this time are to be found in the throat and ears, the glands, the kidneys, and the heart. In the discussion of each one of these, the prognosis has already been referred to so that it is not necessary to recur to this subject again. The sequelæ rarely affect the prognosis *quoad vitam*. So far as any functional disturbance of the various organs affected is concerned, the prognosis may or may not be bad according to the nature or intensity of the process.

Treatment.

Prophylaxis.

The axiom can be set down, that in order to prevent the spread of scarlatina the patient must be kept from direct and indirect contact with healthy people throughout the course of the disease. While it is easy to make this statement, in practice it involves a multiplicity of conditions extremely difficult to carry out, sometimes impossible. Scarlatina can be limited in its spread very much more readily than some of the other exanthematous diseases. But as has been seen in discussing the etiology of the disease, views differ very widely as to the modes of doing this. The principle to be followed is that of taking the fewest chances compatible with the safety of the patient, so that it will not be astonishing if it is found that the writer holds a middle ground as to the method to be followed in preventing the spread of this disease. For the individual case the method to be applied is the following: The patient is to be removed to a separate room, if possible to the top floor of the building. The room is to be prepared by removing if possible everything that cannot be subjected to the action of boiling hot water. This means that the hangings are to be taken down, the carpet to be raised, pictures and ornaments to be removed, closets emptied, and only such bedding and such clothing to be used as can be treated by boiling hot water or can be destroyed. It is advisable to have a set of dishes supplied to the sick-room and a small gas or gasoline stove, upon which water can be heated to the boiling point at any time for the use of disinfection or the preparation of simple articles of

food. The nurse, or whoever acts as nurse, should be attired in washable uniform, and it must be distinctly understood that if the nurse be a member of the family, he or she must not come in contact, direct or indirect, with any other member of the family. All other methods will fail in preventing the spread of scarlatina. With this method carried out in the strictest way the author has failed but once in preventing the development of a second case of scarlatina in a family, and in this instance he is not positive but that the infection was brought from another case. When should the patient be sent to this room? As soon as the diagnosis of scarlatina can be made. According to the author's opinion this is as soon as the eruption appears and not before. But if, in the presence of scarlatina in the household, any of the other members of the family show evidences of affection of the throat, they should be kept under supervision until a positive diagnosis of the nature of the throat trouble can be made. In such cases it is necessary to remember that scarlatina sine eruptione is just as dangerous as regards the spread of the disease as scarlatina with the eruption. If it occurs that no such room as the one described can be had in a private family, the next best is to select a room which does not communicate with any other and in which the patient and his nurse can be kept as far removed from the other members of the family as possible. It would be well if every city had a large hospital for the reception of patients with scarlatina. In this way undoubtedly epidemics of scarlatina could be thoroughly stamped out. In this way only would it be possible to cut short an epidemic. Unfortunately in one way, and possibly properly in another, with our notions of personal liberty, this plan, namely, the removal of all patients with scarlatina, must be considered as Utopian. When no single room can be obtained in a family, the best that can be done in order to prevent the spread of the disease will only be a compromise.

Shall the healthy children be sent away from the house? By all means, if this is possible. Two things are accomplished in this way: greater freedom is given to those that remain in the house, therefore greater care to the patient, and the danger of infection of the other members of the family is lessened. But it will be asked, Are not the chances of the spread of the infection greater when the healthy members of the family, who have already been exposed, are spread over other houses? This question can be answered most positively in the negative. As has been stated before, the author's experience with the contagiousness of scarlatina in the period of invasion leads him to the positive conclusion that at that time the disease is very little contagious. Notwithstanding the statements that have been made

by v. Kerschensteiner and Vogl, the author still adheres to the view expressed, and while not doubting the experiences of these and other observers, he must still insist upon the value of his own observations (see the section on Etiology).

A question that is very pertinent in this connection is the one whether school shall be closed or not during the prevalence of an epidemic. This can be answered yes or no, depending principally upon the nature of the school and its locality. For country districts, in which the children have to come long distances in order to reach the school, isolation is probably best effected by closure of the schools. In cities, on the other hand, especially in crowded districts, little would be gained in this direction by closing the schools. Take, for instance, a large tenement district in which there are forty, sixty, or even a greater number of families living close together, isolation would be practically impossible. The children will play together so long as they are well. When they are ill, if sufficiently so, they are kept in bed; as soon as they are able to be up, they are again sent out, especially during the most contagious period of the disease. So that, so far as isolation is concerned, in cities certainly nothing is gained by keeping the children away from school. Again, the advantages of sending them to school in the presence of an epidemic are to be looked at. As soon as they are ill they are sent home, and in the majority of cases this occurs during the period of invasion, when they cannot infect other children. With a wise teacher they are not allowed to come back to school until desquamation has been completed. Again, with the methods of sanitation that are in vogue in a great many of our large cities, when these cases are reported to the health officer, as they will be when a child is absent from school, the patient is not allowed to return until permission to that effect is given to the parents, and at the same time official notification is given to the teacher that the patient is now well and no longer able to spread the disease. The best method and the one that presents a certain degree of security in keeping the schools open, is the one now employed in some of the large cities of this country, namely, of having all the children inspected by a physician before they are allowed to enter the schoolroom. The results of this method are extremely encouraging and when applied, in addition to proper vigilance at home, the keeping of the schools open in cities, instead of increasing the spread of an epidemic, will tend to its breaking up.

Prophylaxis by administering medicines of any sort must be looked upon with doubt, it matters not from what source statements regarding its efficacy come. It has been the custom for a long time for a certain class of practitioners to give belladonna in order to pro-

tect their patients. This method is based upon the homœopathic doctrine. Latterly other remedies have been recommended. If a glance be taken at the percentage referred to before in connection with epidemics in the Faroë Islands, it will be seen that with any remedy we should not be justified in concluding that there was any efficacy in the remedy even if a large number of individuals was not attacked by scarlatina. It is impossible, therefore, either to assert or to deny the efficacy of any procedure in preventing attacks of scarlet fever, except the ones referred to above. It certainly seems to be trifling with danger to rely on the internal administration of any remedy that we have at the present time to increase immunity to the scarlatinal poison. When the protective agencies of the human system shall have become isolated, then it will be time to speak of producing temporary immunity. For the present, in the absence of knowledge in regard to the poison and its anti-poison, every procedure of this kind must be looked upon in the light of an experiment and one based purely upon empiricism, not scientific reasoning.

How long shall the patient be kept away from others? A safe rule to follow is never to permit a patient to come in contact with healthy human beings until desquamation is completely ended. In the majority of instances this will not be before the termination of the sixth week. The above rule may require a certain amount of explanation in that it is known that one part of the skin or another may continue in a condition of desquamation for a long time after the real process of desquamation has ceased. So that the term desquamation is meant to imply the first desquamation. Successive peelings of the skin are not to be looked upon as belonging to the process of desquamation *strictissimo sensu.*

Another question that comes up in connection with this rule is: What shall we do in cases in which the desquamation is very slight or not to be noticed at all? In these cases the term of seclusion may be reduced with safety to four weeks, but no case of scarlatina, however mild it may be, should be allowed to expose others before the termination of the fourth week. Much sinning is done in this direction by the profession. The terms scarlet rash, scarlatina, scarlet fever, malignant scarlatina are used not only to signify differences in intensity of the process but also differences as to the possibility of conveying contagion. It needs only a reminder to make the fact plain that all these various forms are due to one and the same poison, and whatever may be the result so far as the individual is concerned, he is capable of transmitting the disease, whether it shall have been a light attack or a very severe one. Indeed, as a matter of fact, it is usually the light cases that convey contagion,

for the simple reason that they have not been confined for a sufficient length of time.

For *disinfection* it will be well to use a definite method. As far as the patient himself is concerned, if the procedures that are recommended under the heading of hygiene shall have been carried out, all that will be necessary when he leaves the sick-room will be to give him a bath, to wash the hairy parts with soap and water and then alcohol, after which he may be allowed to come in contact with the other members of the family. So far as the surroundings are concerned, the task is a very much more difficult one. The rule of the author has been to subject everything that has been in contact with the patient to the action of high temperature—in other words, to disinfect either by steam or by boiling hot water. We have no scientific assurance of the efficacy of any other disinfectant, as has been stated before. It is true there are some things, as will be seen, that cannot be subjected to the temperature of steam in a private residence. Here a certain amount of risk must be taken, but a very minimal one. The method that is referred to is as follows:

The clothes of the patient and the nurse must be either destroyed or boiled. All the bed clothing must either again be boiled or be destroyed; for the bedding the latter procedure is the best. If, however, there can be found a large sterilizing apparatus, such as should be connected with every hospital, exposure to the temperature of steam or superheated steam for one hour will be sufficient to destroy the poison. The carpets having been taken up, it is not necessary to dwell upon their disinfection. In case the removal of carpets from the room should not have been feasible, they also must be subjected to the action of steam. Washing with any disinfectant is tentative. Beating them is neither sufficient nor safe to others. The difficult part in disinfection is found in the room itself. The author's method has been the following: In case the walls are papered, the paper is to be thoroughly rubbed off with dough to which there has been added a solution of corrosive sublimate. The masses of dough that fall off as the result of rubbing are to be carefully collected and then burned. Then a new coat of paper is to be put upon the wall so cleansed. This applies for the walls as well as for the ceilings. In case both walls and ceilings are painted, the same process of rubbing is to be gone through with; this to be followed by a new coat of paint. The best possible results can be obtained when the walls and ceilings are whitewashed or kalsomined. Then a new coat can be put upon the walls and ceilings. The floor is to be thoroughly scrubbed again with a solution of sublimate and soap and water, and if possible either to be painted freshly or varnished. All toys and

books that have been used to amuse the patient must either be treated by boiling hot water to effect sterilization, or, if this is not possible, must be destroyed. After all this is done, it is wisest to open all the windows, to lock all the doors, and to allow the room to be untenanted for at least one week, if possible longer.

The question now arises: What will be the result of any method of room disinfection? Vogl and Hagenbach-Burckhardt have reported very bad results, the former in military, the latter in civil practice. The conclusions that they arrive at are that it is impossible to render a room sterile, so far as scarlatinal poison is concerned. It must be confessed that the methods that they have employed have been apparently sufficiently thorough to warrant better results. But the suspicion remains that these methods were not carried out with sufficient exactness, for the author's experience with the method just described, one used for the last twenty years, warrants him in the conclusion that complete disinfection of the room is not only possible but feasible. In all his experience in private practice and in children's hospitals properly equipped, he has never found it difficult to carry out the proper disinfection of a room, and he may state that in no instance in his experience has a patient become infected as the result of occupying a room in which there had been a scarlet-fever patient.

That scarlatina is carried by nurses and physicians has already been shown. The nurse, if properly equipped and properly trained, needs very little admonition and teaching to prevent her from disseminating the disease. She must, in the sick-room, always wear washable clothes and always have her hair covered. After this a bath, thorough cleansing of the hands, washing of the hair with alcohol, and a change of clothes will be all that is necessary to prevent her from subjecting others to the contagion. With physicians the problem seems to be a more difficult one. There is no one in large practice who has not seen cases in which a physician has transmitted scarlatina. Indeed, very few of us have been fortunate enough to go through with many years of practice, handling a great deal of scarlatina, without having to accuse himself in one way or another of having transmitted this infection. If every physician, certainly in former days, were to hold a strict account with himself in regard to this matter, the conclusion would undoubtedly be the above. It is a curious manifestation of the times that in order to open an abscess, the physician will go through with the most complex and complicated manipulations for sterilization of his patient and of himself, and yet will not take the trouble to change his clothes when going to see a patient with scarlet fever, nor so arrange his rounds that he does not

see patients, especially children, after having attended a case of scarlatina. It is admitted on all hands that for the physician having an extensive practice, the matter of self-disinfection is a very difficult thing, consuming a great deal of time, and sometimes nearly impossible; and yet, when the risks are taken into consideration, no labor should be thought too great in order to prevent dissemination of this treacherous disease.

The least that one can expect of a physician is that he change his outer clothing when going to see a patient with scarlatina; the utmost that one can expect is complete sterilization of himself. As the poison of scarlatina can be limited, the latter undoubtedly is unnecessary; the former, however, is absolutely imperative. Whether the outer clothing used in the sick-room be of rubber or of washable material is comparatively immaterial. All that is required is that whatever comes in contact with the patient can be thoroughly cleansed. This holds good not only for the physician himself but for the instruments used—thermometer, stethoscope, etc.—in the examination of his patient. The question whether a physician attending cases of scarlatina should also attend puerperal cases is one that must be left to the medical conscience of the physican himself, and to his faith in his ability to render himself completely sterile. There can be no doubt of the fact that in the presence of an epidemic of scarlatina, if possible the safest plan is for the physician to give up his puerperal cases. On the other hand, consideration must be taken of the fact that in many localities and for various reasons it becomes imperative for the physician to attend to both scarlatinal cases and obstetrical cases. In the latter case it is impossible for the physician to be too careful, as far as he himself is concerned.

All the rules given above will of necessity require more or less modifications at times. When such is the case, those things are to be done that are most important. Frequently, in actual practice, very little can be done to prevent the spread of the disease.

General Hygiene.

A room should be chosen in which there is plenty of air and plenty of light. In regard to the former, we are now most of us coming to the conclusion that plenty of air does not hurt the scarlatinal patient, so that ventilation should be properly attended to by opening windows. More and more are we coming to the conclusion that the much-feared "catching cold" plays no rôle in the etiology of complications in scarlet fever. If the physician is afraid of exposing his patient to draughts, the windows may still be opened and

the patient may be protected by screens. Some deference must be paid to public opinion, which in matters medical is always the result of our own teachings. Wherever this fear of "catching cold" is very pronounced, there, without subjecting the patient to the dangers of an ill-ventilated apartment, concessions may be made in the way of screens and the protection against draughts by other means. After all, we are not in a position to state that a given case will not have certain complications, and in the absence of etiological information, with laymen, when certain complications, especially in the upper respiratory tract, develop, the first conclusion arrived at will be that the patient has been subjected to the dangers of "catching cold." The temperature of the room should be kept at between 65° and 70°. When this can be done by means of an open fireplace, we have the best possible combination for keeping the air clean and fresh. The patient should be kept in bed. After what has been said in regard to "catching cold," this will seem paradoxical, and yet after a moment's reflection it will be found that this is a method of treatment perfectly logical.

We know that movement, therefore functional activity, predisposes to the localization of certain infectious agencies. We know, furthermore, that as the result of increased metabolism (resulting from motion) effete matters are produced which must be eliminated by the organ which we are most anxious to protect and to which we wish to give as little work as possible—the kidneys. For the same reason an equable temperature of the skin, which can be attained only by keeping the patient in bed, while it does not have any effect in preventing or producing inflammatory changes, will certainly give to the kidneys less work than when the patient is allowed to change temperatures constantly, for the simple reason that the insensible perspiration is increased by keeping the skin at a comparatively high temperature. It is not meant that the patient shall be kept in the condition of sweating. Indeed, the covering should be as light as the external temperature will permit. It must be remembered that in the olden days Heim, treating his patients with enormous bed covering, closed windows, and high atmospheric temperature, was enabled to make the diagnosis of the acute exanthemata when he entered the door of his patient's house. With our modern method of treatment, no one any longer speaks of the characteristic odor of the exanthemata.

The hygiene of the mouth is of the utmost importance, both for the patient and for his surroundings. It will be remembered, as stated in the etiology, that the sore throat is looked upon as bearing the same relation to scarlatina as the primary sore does to syphilis.

However this may be, undoubtedly much can be done to prevent the development of streptococcus infection by properly applied treatment of the mouth. When salicylic acid was first introduced as a specific in scarlatina, the writer clinically made of its use a routine method in the treatment of all cases of scarlatina that required treatment. This was done not so much in the belief that salicylic acid was to be looked upon as a specific, but principally on account of the fact that it is a most admirable disinfectant for the mouth, and, as subsequent developments have shown, especially inimical to the streptococcus. According to the age of the patient, it has been my custom to administer one teaspoonful of 0.5 per cent. to 1.5 per cent. solution of salicylate of soda every hour for the first two to four days of the disease. This method is especially valuable in very young children who cannot gargle and in whom the application of an atomizer frequently meets with violent resistance, probably doing more harm than good. When the patient is able to gargle, one of the best mouth disinfectants that can be used is listerine; a mild solution of permanganate of potash or a solution of borax or boracic acid, an alkaline solution, is frequently to be preferred. If evidences of streptococcus infection are already present, mild solutions of hydrogen dioxide can be used to great advantage. For inhalations the same remedies can be used; the oil of eucalyptus may be added with great advantage. In children the author has always had a more or less wholesome fear of using either potassium chlorate or carbolic acid.

The skin requires especial attention, on account both of the subjective symptoms and of the danger of spreading the disease by means of the scales being allowed to fly about the room. Both of these indications are met, first by inunctions and secondly by baths. For the purpose of inunction, a clean non-acid fat must be selected. A very good article for this purpose is cacao butter or lanolin. Vaseline should not be used in very young children, as it produces irritation of the skin. In those cases in which itching is very great, much benefit may be obtained by the addition of small quantities of menthol, one to two per cent. All other additions seem unnecessary. Certainly it is impossible, as has been stated before, to sterilize the scales by the use of disinfectants. Carbolic acid especially must not be used in children, for the danger of this acid is greater than the benefit derived from its use. As soon as desquamation begins, the patient should have a lukewarm bath daily. After being thoroughly dried, he is to be anointed by whatever form of fat may be chosen and then put to bed again. Schneemann attributed specific properties to this method of inunction. The indications for it, however, are not those of a specific method but simply those stated.

The feeding of scarlet fever patients is one concerning which there is much diversity of opinion. During the period of invasion the question as a rule settles itself. The patient will not require any feeding, as he has continual vomiting. When the eruption appears, then comes the question of feeding. Some authors claim that the best results are obtained by a milk diet. Thus, Jaccoud makes the statement that in fifteen years since he has adopted the method of milk feeding, he has not seen a case of nephritis after scarlatina. Upon the other hand, in looking over the statistics of scarlatinal nephritis, it will be seen that those authors who have not insisted upon a strict milk diet, while not claiming such brilliant results, do not have worse results than those who advocate the method of milk feeding alone. It has been the habit of the author to give to patients with scarlatina, during the first week of the disease, a diet limited solely by the digestibility of the various articles.

Such diet is to be given as would be ordinarily given to a patient in bed; therefore not too much meat, not too many carbohydrates. With the beginning of the second week of the disease, the writer has always put his patients upon an absolute milk diet, and this for several reasons. First, it is necessary, almost imperative, that as much fluid be introduced into the scarlatinal patient as possible. The kidneys are best flushed, urea is eliminated in larger quantities, and more fluid is supplied for insensible perspiration. Furthermore, it has been repeatedly shown that milk, when subjected to the action of bacteria, will produce fewer harmful end-products of digestion than any other article of food. So that when we are giving milk, we are doing the best for our patient, first, in the matter of feeding; second, in the matter of supplying fluids; third, by way of more or less sterility of the intestinal tract, therefore less risk of autoinfection. In addition to the milk, as much pure water as possible should be given. Whether this be in the form of distilled, aërated, or the many mineral waters that are pure waters, is immaterial. This method of feeding is continued until the end of the fourth week, when carbohydrates are first tried; if these do no harm, meat is tried, and this is quickly followed up by a return to the usual diet. The daily examination of the urine is the only means by which we are enabled to tell whether the diet list shall be increased or not.

Medical Treatment.

As has been so often repeated, not knowing the cause of scarlet fever, we are limited in all respects, and not the least in the way of treatment. We have no specific method of treating scarlet fever.

While in certain directions advances have been made in connection with prophylaxis and the treatment of complications, in other respects our treatment remains as it has been for so many years, purely symptomatic. This could be expected, considering the progress that has been made during the last twenty-five years in therapy. Mild cases require no treatment, except that which has been referred to in the preceding sections. One of the methods that borders on the specific, in that in a certain way it is causal, can be referred to in the present connection. This is the treatment of complications by Marmorek's streptococcus serum. Theoretically objections must be raised to this method of treatment from the point of view that the streptococcus pyogenes is in all probability not the cause of scarlatina; so that from the point of view of etiology, we cannot accept a streptococcus serum of Marmorek, or any serum gained in the same way as Marmorek's, to act except in relation to certain complications of scarlatina. The serum, furthermore, is deficient in that we know that the streptococcus pyogenes is not the only streptococcus that produces complications in scarlatina; so that, in order to overcome these complications, it would be necessary to have serum from animals immunized against a great variety of streptococcus forms. These, in brief, are the theoretical objections to the use of Marmorek's serum.

As a matter of fact the Viennese school of hygienists, especially Paltauf, have already proven that immunization against one form of streptococcus does not produce immunity against others. So far as the practical application of the Marmorek serum is concerned, we may say that in certain cases it does astonishingly well, and in others, on the other hand, it produces no results. This has been the experience of the writer. In the last few years he has made it the routine practice to treat all scarlatina patients that came under his observation with streptococcus serum. While the number of cases has been comparatively few, he has come to the distinct conclusion that the serum does not affect the course of the disease in any way, that those forms of malignant cases in which there is an overwhelming with the poison are not modified in the least, but that occasionally the local symptoms of streptococcus diphtheria are affected most remarkably. I have seen one patient recover from streptococcus diphtheria after the use of the streptococcus serum, in whom the membrane extended from the tip of the tongue to the middle ear and in whom the whole mouth was covered with this thick streptoccocus membrane accompanied by the usual constitutional symptoms. It is the first time in my experience that recovery has occurred in a case of this nature, and I have no doubt in my own mind that the recovery

of this patient was due to the streptococcus serum. And yet it is too early to decide upon the therapeutic value of this serum. On the other hand, the theoretical objections offered above must not be forgotten. When the streptococcus of scarlatina, if there be such, is found, then our results will be better. At the present time only those streptococcus manifestations can be combated by this serum that are produced by the streptococcus pyogenes. The question of its use in every case is one that can be answered in the negative. The question when it is to be used, is to be answered when there are serious complications produced by the streptococcus pyogenes.

From a theoretical point of view no class of diseases should offer greater promise of results from specific therapy than the acute exanthemata. Experiments have been made in this direction by Weissbecker, by Kelaïdites, and by Huber and Blumenthal. The latter obtained certain results in scarlet fever, measles, pneumonia, and erysipelas by injection of serum obtained from the blood of patients convalescent from these diseases. In scarlatina the blood was taken by means of venesection from four to twenty-one days after fever had disappeared. The method is as follows: 100–150 c.c. of blood are immediately diluted with equal parts of a sterile normal salt solution, then there is added one per cent. of chloroform, and the whole is shaken up and allowed to stand for twenty-four hours. It is then pressed through sterile linen and filtered through a Berkefeld-Nordmeyer apparatus. A clear, dark-red fluid is obtained which is sterile and remains so for at least ten months. Thirteen cases of scarlatina were injected with 20–40 c.c. of this fluid, twelve of them on the following days of the disease: 2 cases on the second day; 4 cases on the third day; 3 cases on the fourth day; 2 cases on the fifth day; 1 case on the sixth day. In 3 cases a positive and most beneficial result was produced; 1 case could not be taken into consideration on account of complication with puerperal pyæmia and parametritis; in 8 cases results were not very pronounced, and in 1 case no effect was produced, although the patient had received 40 c.c. of the serum. As far as temperature is concerned the decline began on an average upon the sixth or seventh day, never later; normal temperature was found three times on the fifth day of the disease, twice on the sixth, seventh, eighth, and ninth days each, and once on the tenth day, never later. When lysis took place after the injection it occurred seven times upon the first and three on the second day of the injection, never later. The exanthem continued to develop in 6 cases after the injection, which in some cases was followed by a slight, temporary rise in temperature. No serious complications were observed; in 3 cases pains in the joints were noted.

Fever.

At the present time we no longer look upon fever as the all-important symptom to be combated, but nevertheless no physician considers himself justified in standing by and seeing the temperature above danger line day in and day out without attempting to do something to reduce the fever. This is not the place to enter into the discussion of this broad subject, so that we will simply state that the rule in scarlatina is that when the temperature goes to 104° in the rectum and remains at this height, something should be done in order to cause its reduction. There are two methods that are used in the treatment of high temperatures, the one hydrotherapy, which is coming more and more to the foreground; the other, the so-called antipyretics. Scarlet fever was one of the first diseases to be treated by hydrotherapy. In 1798 Currie began to use this method, and he did more to overcome the prejudice in regard to "catching cold" than possibly anybody else. In 1801, in a severe epidemic in Liverpool, he treated over one hundred and fifty children, including his own, and, as he says, was very much surprised by the excellent results.

The attempt has been made to make a method of the treatment of scarlatina by cold baths, as has been done for typhoid fever by Brandt. For reasons that it is not necessary to detail here, this has been a complete failure. The principal reason that can be adduced is that mild cases do not require anything like the severe methods that are applied by the hydrotherapeutists, and the malignant cases are not saved by it. On the other hand, it is barely possible, so far as this country is concerned, that the strict method by hydrotherapy has not had a fair trial. It may be remembered how long it took the Brandt treatment of typhoid fever to gain a foothold in this country. The making of a method, therefore, in scarlatina may do something to advance hydrotherapy, and possibly our conclusions after extended experience may require revision. The method consists in bathing the patient every two hours, whenever his temperature goes to 104°, the temperature of the water varying, being in older children 16° C. (59° F.), in younger children 20° C. (68° F.). This is to be kept up day and night. After the bath the patient is to be put to bed. According to the intensity of the disease, the hydropathic measures can be modified. In milder cases the baths can be made warmer, up to lukewarm. In cases requiring still less interference, or if for any reason these baths cannot be given, the pack may be used. As a matter of fact the cold pack frequently reduces temperature when the bath does not, so that in a certain way the cold pack is not to be looked upon as a reduction in the process of bathing or as productive of fewer or less results. In milder cases still, spong-

ing with lukewarm water or water and alcohol may produce the desired effect. On the other hand, in very severe cases, additional hydrotherapeutic measures have been used. When there is much involvement of the brain as shown by sopor, stupor, or even coma, it has been found advantageous to put the patient into the cold bath and then pour very cold water upon his head. The physician must use this method with care and with judgment. To the on-looker the method seems a cruel one, and if the physician is in the presence of what seems to be a fatal issue, it must be left to his judgment whether he can use these harsher methods of hydrotherapy or not. It would be better to use the ice-bag to the head, which produces very little effect as a rule, or the cold coil, which is highly recommended by some authors. The other nervous symptoms, especially restlessness, jactitation, twitching, convulsions, are best treated by a bath of at least 110° F., in which the patient may be allowed to remain for five to ten minutes, then taken out, without drying, and put into bed and thoroughly wrapped up. If the convulsions occur with low external temperature, the patient must be thoroughly dried before being put to bed. Jürgensen mentions the following conditions as contraindications to the cold bath: (1) All thoroughly well-developed conditions of heart weakness, immaterial from what cause, when it is impossible by means of stimulants to improve the function of the heart; under this heading he includes anatomical changes, especially inflammatory changes in the heart; usually, as he says, there is a pancarditis. (2) All conditions of dyspnœa accompanied by narrowing of the upper air passages. (3) Hemorrhages from the nose or throat, from eroded blood-vessels, and in the hemorrhagic diathesis. (4) All inflammations of joints; as no especial improvement can be expected from this method of treatment, the pain of movement must be spared the patient. He says that upon the whole these are the contraindications put down by Leichtenstern. The writer would like to add that these cold baths are never to be used in the case of young infants, and that this contraindication is almost an imperative one.

So far as the treatment with antipyretics is concerned, the tide has now turned against them. It is interesting to see the comparative enthusiasm of Ziemssen as to the use of antipyretics in 1888, and the disapproval of their use by Jürgensen in 1896. The only one of the coal-tar products that Jürgensen wishes to be used is phenacetin and then merely in connection with special conditions. He says that he has gotten the impression that phenacetin does good especially in conditions of sepsis. Again here it would lead us too far to discuss the reasons for this rapid fall into disfavor of the coal-tar products.

Not a little is due to the fact that our notions of the importance of increased temperature have been largely changed in the last ten or fifteen years in that the fever nowadays is no longer looked upon as the essential feature of the disease; but not a little is owing to the fact that the effect of all these coal-tar products is more or less depressing, sometimes very greatly so, and that certain changes are produced by all of them in the blood, which render its most important function less active than under normal circumstances. We refer here to the production of methæmoglobin. It is only in urgent cases and when it seems possible to produce a certain effect upon the nervous system, that acetanilid, antipyrin, or phenacetin is still used. Of the three phenacetin is by far the safest. The writer has for several years given up the use of these antipyretics for the control of temperature.

Treatment of General Infection.

Within the last five or six years a method has been introduced for the treatment of the constitutional symptoms which, from a theoretical point of view, seems to promise very much. It consists in the dilution of the blood so as to render toxins that are circulating in it less effective. This can be accomplished in one of various ways: first, by hypodermoclysis or by injection into the serous cavities of a sterilized normal saline solution; secondly, by the introduction into a vein of this same solution; thirdly, by contemporaneous bleeding and injection of a saline solution into a vein (*lavage du sang*). The methods designated above are to be used in the cases of varying intensity. They can be used in any form of blood poisoning, in the strict sense of the word, whether this blood poisoning be due to an accumulation of toxins or to that general combination of symptoms called uræmia. The indications for their use in specific cases would be those that can be called malignant and those in which the symptoms of uræmia seem to be so threatening as to endanger life. In regard to the malignant cases the difficulty in the use of this method seems to the writer to be that we cannot be positive when we are dealing with a malignant case early enough to prevent the lesions that are produced by the toxins, which cause a fatal result. But at all events the method even in these cases deserves a trial. In uræmia the position is a different one. It certainly seems that in bad cases of uræmia this method should be given a trial. While the author's results with the method have not been so satisfactory as might theoretically have been expected, his experience is as yet too limited to permit him to pass a final verdict upon its use.

Stimulation.

It is a great mistake to imagine that every case of scarlet fever requires the routine use of alcohol. The reason for this can be summed up in a few words. The duration of fever in ordinary cases is comparatively short. If it be treated according to the methods indicated above, the fever will do little damage. Therefore the use of alcohol as a food seems unnecessary, certainly not so necessary as it is in long-continued fevers like typhoid fever. Alcohol is eliminated partly by means of the kidneys. The possible prevention of kidney troubles is one of the objects of our treatment. It is unnecessary, therefore, to add to the risks of irritating the kidney by means of our therapeutic measures. By some the use of large quantities of alcohol has been advocated in the treatment of so-called malignant cases. Like so many other measures, this has always failed in the author's experience when applied to these cases. It is far better, when stimulants are required as such, to use those other remedies that will be referred to in connection with complications on the part of the heart.

Treatment of Complications.

Throat and Nose Troubles.—Too much stress cannot be laid upon the prevention of throat troubles, as has been already mentioned in connection with hygiene. Not only do we, by the measures recommended, prevent throat troubles themselves, but we prevent that which is of much greater importance, secondary infection. Hutinel has made the point that in one hundred cases of scarlatina he has had neither a death nor secondary complications, simply on account of the use of antisepsis as applied to the throat. While this statement may be a little too enthusiastic, certainly our results in scarlatina, when these hygienic measures are applied, are far better than they were in the pre-antiseptic days. As soon as throat trouble begins to develop in the form of spots or a membrane, active measures should be taken. This can be done most effectively by local treatment which has been applied in a great many different ways: by gargling, douching, local applications in the form of a spray, or direct application to the parts affected. Gargling is a method not to be relied upon. The douche can be used to great advantage, but serious objections can be made to it on account of the unpleasantness connected with its application, especially in young children. By it a large quantity of fluid is introduced into the mouth under comparatively low pressure. Solutions of various drugs may be used, first and foremost the salicylate of sodium, boric acid, eucalyptus, or any of the mild

antiseptics. The only advantage to be gained by this method is that frequently the fluid will enter the pharynx and wash out the nose from behind. In cases of streptococcus diphtheria of the nose, this method may become a very valuable one. The spray is a method that can be used under all circumstances; even in the most refractory child, atomizing the throat can usually be effectually done, the only contraindications being in conditions in which there is great weakness or resistance on the part of the patient. In using the spray, alkaline solutions, hydrogen dioxide, or again any of the milder non-irritating antiseptics can be used. The best method is the direct application, by means of a cotton swab, of the remedies that are to be used to the parts affected. First and foremost among these comes the use of Löffler's iron toluol solution. There is no doubt of the efficacy of this remedy when properly applied. It should be used once or twice in twenty-four hours, and the cotton should be held in contact with the diseased parts a sufficient length of time in order to insure the efficacy of the application. The objections to it are the pain that is produced and not infrequently a certain amount of irritation. Next to this in efficacy comes the application of hydrogen dioxide. For this purpose a three-per-cent. solution can be taken, which can be applied not oftener than twice in the twenty-four hours by the nurse, depending upon the developments of the local symptoms. When the membrane spreads beyond the tonsils, it becomes necessary to determine by culture the nature of the complication. In case it is due to the Löffler-Klebs bacillus, large doses of antitoxin should be injected as soon as possible. When the Löffler-Klebs bacillus is not found, the serum of Marmorek, or equally good, the streptococcus serum such as is prepared in this country by Parke, Davis & Co., should be used immediately. It will be astonishing, in some very bad cases, what good results will follow its use.

For the treatment of the nose, as well as for the treatment of the mouth, local applications are necessary. The use of the nasal douche is associated with certain risks. But in the majority of instances of scarlet fever it will be found necessary to use this method, unless douching of the mouth does the work, because it is manifestly impossible to wash out the nose with sufficient frequency in a small child and not do damage. In the treatment of the nose only the mildest fluids are to be used. Indeed, excellent results have been reported simply with the use of cold water. The hydrogen dioxide may be used in very weak solution; but the use of the Löffler solution in the nose would be attended with too great risk, applied in any way. Whatever remedies are employed in the treatment of the mouth, the throat, or the nose, care should be taken not to use anything that is

very irritating. The application of strong solutions of nitrate of silver or solid nitrate of silver itself has been discarded. Huebner has recommended the use of carbolic acid injected into the tissues of the tonsil or the soft palate. At the present time this has been rendered unnecessary; at any time the risk of introducing a large quantity of carbolic acid into the system of a child seems to the writer to be greater than the benefits coming from its use.

In the case of gangrenous sore throat, active destruction of the parts affected might be thought of. This should be done according to the method recommended by the author in the treatment of noma, by means either of the galvanocautery or of the Paquelin cautery. Whichever of these two is used, the tissue should be destroyed regardless of results, unless large blood-vessels are thereby endangered. Unfortunately the proximity of one of these vessels will, in a great number of cases, prevent free cauterization and thus prevent the accomplishment of much good by this method.

The Ears.—The ears should always be watched in all scarlatinal cases in which there is a decided complication on the part of the throat. In very young children the diagnosis of ear trouble is accompanied by great difficulty, so that it becomes the duty of the practitioner to examine the external ear daily by means of proper light. As soon as there is bulging of the drum membrane, a perforation should be made so as to give vent to the exudation, to prevent symptoms of pressure in directions that may become dangerous, and to have a pus cavity to deal with which can empty itself and which can be treated locally. If involvement of the mastoid region has taken place, or if free drainage of the pus cavity is not effected, the mastoid operation should be performed. The local treatment must consist in the use of non-irritating antiseptics. These can be applied in various ways, either directly upon cotton or in the form of solutions or powders, the latter being the safer and more convenient method. Here, again, the maxim of *nil nocere* must not be lost sight of; for this reason inflation by means of the Eustachian catheter or by Politzer's method must be used with great caution and only in those cases in which positive indications for it exist.

The Lymphatics.—A moderate amount of enlargement of the lymphatics requires no special attention. When, however, the first fever having disappeared, the lymphatics become more swollen and painful, and fever again appears, active measures should be taken, first to control the inflammation, and secondly, if this is no longer possible, to cause the process of suppuration to be completed as soon as possible, so that an abscess may be treated according to surgical rules. In connection with the first indication, the ice-bag and pressure are to

be used; the ice-bag is to be kept in contact with the enlarged gland day and night, a thin layer of flannel being interposed so that the irritating effect upon the skin may be reduced to the minimum. Pressure is best applied by means of collodion. Flexible collodion should be painted over the gland and some distance beyond it, twice or three times a day until there is produced a thick membrane, whose continuity is to be constantly kept up by repeated applications of the collodion. In view of the application of collodion in limiting erysipelas, it seems that a second indication for its use can be found in that it prevents the absorption of materials by the superficial lymphatics. However this may be, certainly in the long experience of the author, he has never had to deal with a case of angina Ludovici when using this method. The ice-bag, protected with the flannel, is to be kept on at the same time that the painting with collodion continues. If the patient continues with fever and sweating, the gland not becoming smaller, the ice-bag must be discarded and poultices should be applied, the collodion still being continued. At this stage it is more important to paint the surroundings of the gland with collodion than the gland itself.

As soon as the first evidences of fluctuation present themselves, an incision must be made into the gland. This cannot be done too early. Indeed, it has been a question in the mind of the author whether after the lapse of three or four days of poulticing an incision should not be made even without the evidence of fluctuation. By this method the gland, which already has a tendency to break down, would break down in the neighborhood of the incision and the pus, which is present only in minute quantities in the trabeculæ, on account of the anatomical structure of the gland would eventually find its way into this incision. When the incision has been made, the poultices should be kept up, all proper attention being directed to asepsis. At this time the general treatment of the patient requires chalybeates. Indeed, it is a question whether in most cases of scarlatina the administration of some iron or blood preparation is not of great advantage, as in no acute disease does both the corpuscular part of the blood and its coloring matter suffer so great destruction. If notwithstanding the precautions just mentioned infection of the cellular tissue does take place, free incision should be made to evacuate the pus and to prevent further infection. The use of iodoform in this condition has been highly recommended. But after all the proper indication is to get rid of the pus. For the treatment of enlarged lymphatics following scarlatina, nothing has accomplished so much for the author as the use of pure creosote in moderately large doses, one-half to one or two minims three times a day.

Kidneys.—The treatment of nephritis has been partly outlined in connection with the hygiene of scarlet fever; rest in bed and a milk diet are the principal things we rely upon. If the anæmia during the course of the nephritis becomes too great, we may use iron preparations, especially the tincture of the chloride, which seems to have a most excellent effect upon the combination of anæmia with nephritis. Diuretics can be used, but they will be found to give comparatively slight results. The best diuretic is water given in large quantities. Lemonade or any of the fruit acids can be used, the former, if constipation be present, with the addition of some saline remedy, especially Rochelle salts. Diuretin has proved a failure in the hands of the author in this form of kidney trouble. Digitalis, highly recommended by some, has not seemed necessary. The bowels should be carefully attended to, best by the use of salines, Rochelle salts, citrate of magnesia, Seidlitz powder (the latter can be made very attractive to a child by the addition of some raspberry syrup), or any other saline. Calomel, in view of its irritating effects upon the kidney, should be used with caution. When symptoms of uræmia appear, the treatment must become more active. In this condition we appeal first to the skin, in order to help in the elimination of the waste products. The patient is put into a bath of 105°–110° temperature, kept there for from ten to fifteen minutes, then taken out and put between blankets without being dried. During his stay in the blankets, which should be at least one hour, he is given as much fluid to drink as he will take, preferably warm. At the expiration of one hour the patient is rubbed off under the covers and placed into a warm dry bed without any exertion on his part. If necessary this can be repeated three or four times or even more in the twenty-four hours. The wet pack does not fulfil all the indications of the bath. When the symptoms of uræmia refuse to be benefited by this simple method, the hot-air bath should be used. Such a one can be extemporized in any well-regulated household. One remedy especially, pilocarpine, has been recommended in lieu of the measures just mentioned. It should be used only in such cases in which the simpler methods fail, and then hypodermatically in round doses. The fact must not be lost sight of that pilocarpine, especially in children, may produce serious symptoms of collapse. This can be prevented by the method of Demme, which consists in the administration of an alcoholic stimulant before giving the injection. In case it is impossible for the patient to swallow, the alcohol may be given either by the rectum or subcutaneously. Under no circumstances should pilocarpine be used when there is much secretion in the bronchial tubes, as the tendency to the

production of œdema of the lungs or a blocking up of the bronchial tubes becomes then very great.

With all the remedies mentioned above, the eliminative function of the bowels must also be called upon with increased vigor, depending upon the state of the patient. The production of watery passages can be effected either by salines or by the use of elaterium. Elaterin must be used with great caution, especially in children. When coma comes on, it may be considered advisable to use the methods referred to above under the heading Treatment of General Infection. Uræmic convulsions should be treated with the measures recommended above, but it must be remembered that the convulsions *per se* may do harm (central hemorrhages), and therefore the admonition not to use narcotics should not be heeded. Chloral, either by the mouth or by the rectum, chloroform (not ether), and lastly, hypodermic injections of morphine should be used in case of necessity. The dropsy under certain circumstances requires especial treatment. When the anarsarca is very great and it seems as if the enfeebled heart were meeting with too great resistance on the part of the overfilled lymphatics of the skin and connective tissue, punctures of the extremities should be made. Not only are these indications met by this method but large quantities of urea are gotten rid of in the fluid that exudes from the punctures. Great care must be exercised by the physician in watching the serous cavities. Hydropericardium, hydrothorax especially, should meet with immediate attention by way of aspiration. Many a patient with renal trouble has been left comparatively well on one day, has been found in an extremely critical condition the next, and has died on the third day, simply on account of neglect of this precaution. An enfeebled heart cannot be expected to do much work in the presence of the great resistance offered by a large exudation into the pericardium or the pleura. When a cardiac tonic is required, strophanthus has seemed to the author to combine the effects of a tonic with that of a diuretic.

The Heart.—The conditions of threatened heart incompetency require energetic and quick action. As a rule, but not always, we may be guided by the condition of the liver. When this organ begins to enlarge suddenly and very much, some trouble with the circulation can be feared. Before this, not infrequently the characters of the pulse, as described before, may give us valuable information. Whether digitalis should be used when we suspect trouble of this sort is a debatable matter. Slow of action, comparatively unreliable, it has seemed to the author not to fulfil the indications of a drug required in the emergency that is to occur. Under the circumstances he prefers the use of strophanthus, but especially the internal

or hypodermic use of nitroglycerin. As a rule, however, we are not called upon to discuss with ourselves the use of a cardiac tonic. We come to the patient and find him in a condition of threatened heart failure. The remedies that are to be used then are hypodermic injections of large doses of strychnine and various stimulants, first and foremost ether, next camphor, or even musk. If the peripheral circulation is very bad, nitroglycerin may be added to the former remedies. Under all circumstances the patient cannot be considered out of danger until the liver has approximately returned to its normal size.

For the treatment of endocarditis, the swallowing of small pieces of ice, the ice-bag over the region of the heart, or, in case the heart's action be seriously interfered with, the use of digitalis is indicated. Mercurials can be used, but always with a great caution. The salicylates should be tried. If pericarditis develops, the mechanical presence of fluid should be carefully watched, as has been indicated before.

Rheumatism.—For the acute articular form, salicylic acid is to be used according to the rules laid down for the treatment of inflammatory rheumatism. Indeed, it is a wise rule to use salicylic acid according to this method tentatively in all cases. If in the course of twenty-four hours, the salicylic acid being given in sufficiently large doses, no effect follows, then we can be reasonably certain that we are not dealing with this form but with the septic form. Care must always be taken in the administration of salicylic-acid preparations. As soon as any of its deleterious effects upon the heart are noticed, its administration should be immediately stopped. Even where no effect is secured by a large doses of salicylic acid within twenty-four hours, unless there be pus present in the joints, it has seemed to the writer that the continued use of small doses of salicylic acid is followed by good results. If there be pus present or if the joint be distended by serous accumulation, aspiration, or under given circumstances opening of the joint may be resorted to. In the presence of grave septic symptoms, the streptococcus serum should be tried. Local applications can be used, either in the form of hot applications of various kinds or otherwise, according to the rules laid down in the treatment of acute inflammatory rheumatism. Especial attention must always be paid to the condition of the heart, the developments on the part of this organ to be treated according to the methods described. Tenosynovitis is best treated locally by the application of ice or, as the case may require, warm applications. The application of mercurials locally in these cases has seemed to prove of benefit in a few cases that have come under the author's observation.

The after-treatment for diseased joints and diseased tendons is of as much importance in order to prevent deformity as is the treatment during the attack. This is to be accomplished according to all the rules and refinements laid down by the orthopædic surgeons.

Gastrointestinal Tract.—The vomiting in the beginning of the attack can sometimes be controlled by one or the other of the following remedies: milk and lime-water equal parts, a teaspoonful to be given every ten to fifteen minutes; the internal administration of carbonated fluids, ice cold and in small quantities (the mineral waters, champagne); the swallowing of cracked ice, care being taken that the ice is not allowed to melt in the mouth; the internal administration of menthol or cocaine in small doses. As a rule the vomiting stops of its own accord and requires no special attention. When the vomiting continues beyond the first thirty-six hours of the attack, it should be looked upon as a bad omen. The diarrhœa that occurs in the beginning of the disease requires very little attention, and then only when it becomes profuse and seems to cause debility. It is then best treated by large doses of subcarbonate or subgallate of bismuth or, in case the stomach bears it, some tannic-acid preparation, best a vegetable tannic-acid preparation, tannate of quinine, and if necessary opium. When the diarrhœa comes from the lower segment of the bowel, a much more serious form, irrigation of the bowel is to be resorted to, using for this purpose the rectal tube or the soft elastic catheter. Large quantities of distilled water or sterilized water to which may be added various antiseptics, especially tannic acid, are to be used. The diarrhœas occurring later in the disease must be treated on the same principles, care being taken not to overlook those patients in whom a milk diet always produces bowel disturbance and therefore is responsible for the condition. In these cases the albumen of egg may be substituted for milk, as well as the vegetable albumins, provided they are not too hard to digest. The diet in these cases must be made up especially of farinaceous substances with eggs and some hæmoglobin-containing substance.

Purpura.—For the malignant attacks of purpura no treatment can be suggested. In the milder attacks the use of fruit acids has seemed to be of benefit in the author's experience. For this purpose lemonade, orange juice, both of which are very grateful to the patient, may be used to great advantage. In such cases the stomatitis usually requires especial attention. As the function of the kidneys is frequently interfered with in these cases, chlorate of potash should not be used. Local applications of potassium permanganate or hydrogen dioxide are sufficient and are usually followed by excellent results. As the purpura may be the forerunner of a cachectic condition or a

part of it, much attention should be paid to the maintenance of good hæmopoiesis. Here the hæmoglobin preparations are especially indicated, hæmol, hæmogallol, ferratin, bovinin, beef juice, in addition to intestinal antiseptics as recommended by the author in another place. The diet should be made as liberal as is consistent with the treatment of the renal complication. If the latter is not present, this question is readily solved. Then the albumins from meats should form the principal article of diet, associated with those recommended above. Even if there be renal complication, provided it is not threatening, the white meats of the fowl can be used tentatively. In twenty-four hours after the administration of one of these albumins the physician will be able to determine whether harm has been done or not. This can be done by examining the urine and by noting the general symptoms.

It hardly seems necessary to speak of *surgical and puerperal scarlatina.* In both of these prophylaxis is more important than treatment. It is in puerperal streptococcus infection especially that Marmorek's serum has been credited with good results.

In the treatment of the *complications with other diseases,* the good judgment of the physician is frequently tested to its utmost limit. The one or the other of the diseases which seems to require most attention must receive it. Fortunately the treatment of the one as a rule is not incompatible with the treatment of the other.

Sequelæ.

Depending upon the condition of the patient, these may or may not require treatment. Patients who have had severe attacks of scarlatina will usually be found in more or less of a debilitated condition. When such is possible, removal to a place in which the climate permits of the patient's being out of doors all the time is advisable, the seashore or the mountains, as the case may demand. The general rules hold good for this form of debility that hold good for all conditions of debility, especial attention in the case of scarlatina being paid to the building up of the constituents of the blood. In case of persistent enlargement of the lymphatic glands all those precautions taken to prevent infection with tuberculosis are especially indicated. The surroundings, the food, and the general hygiene must be carefully looked to in such cases. Indeed when any sequelæ remain, the utmost attention should be paid to the individual as regards both the local and the general treatment; much may be done to make his condition more bearable when the sequelæ are of a serious nature, or to make him a more useful member of society when these are especially of a local nature.

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MEASLES.

BY

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MEASLES.

MEASLES* is an acute infectious disease characterized by a well-marked prodromal stage, by a characteristic eruption, and remarkable for the special tendency to catarrhal inflammation of the mucous membranes.

Both measles and scarlet fever were long confounded with smallpox, and the distinction between scarlet fever and measles has been established only in comparatively modern times. Sydenham[1] was the first to give a clear description of scarlet fever, and to point out the distinction between his "*febris scarlatina*" and measles. His description of the symptoms of measles may still be read with interest and profit, though the reference to pustules must have tended to confuse his readers.

"The measles generally attack children. On the first day they have chills and shivers, and are hot and cold in turns. On the second they have the fever in full—disquietude, thirst, want of appetite, a white (but not a dry) tongue, slight cough, heaviness of the head and eyes, and somnolence. The nose and eyes run continually; and this is the surest sign of measles. To this may be added sneezing, a swelling of the eyelids a little before the eruption, vomiting, and diarrhœa with green stools. These appear more especially during teething-time. The symptoms increase till the fourth day. Then, or sometimes on the fifth, there appear on the face and forehead small red spots, very like the bites of fleas. These increase in number and cluster together, so as to mark the face with large red blotches. They

* The etymology of the word measles is not well settled. Skeat, a very cautious writer of great authority, connects it (Etymological Dictionary) with *maselen* (Dutch), but gives the words *maseles* as fourteenth-century English, and Hirsch ("Handbuch der geographischen und historischen Pathologie") notes the resemblance to *masern* (German) and the Sanskrit *masura* = spots. If the word have these connections it has come into use for the disease in reference to the eruption. Creighton (Lancet, 1896, vol. i., p. 1096) argues in favor of the derivation of the word from *miselli*, a diminutive of *miser*, a term applied to lepers, and accounts for its extension to measles by stating that John of Gaddesdon had confounded the eruption of measles with "the broad dusky red spots on the legs of *pauperes et consumptici*." The French *rougeole* and Italian *rosolia* both have reference to the color of the eruption. The modern Latin term *morbilli*, diminutive of *morbus*, probably had its origin in a comparison of measles with smallpox.

are formed by small papulæ, so slightly elevated above the skin that their prominence can hardly be detected by the eye, but can just be felt by passing the fingers lightly along the skin.

"The spots take hold of the face first, from which they spread to the chest and belly, and afterwards to the legs and ankles. On these parts may be seen broad, red maculæ, on but not above the level of the skin. In measles the eruption does not so thoroughly allay the other symptoms as in smallpox. There is, however, no vomiting after its appearance; nevertheless there is slight cough instead, which, with the fever and the difficulty of breathing, increases. There is also a running from the eyes, somnolence, and want of appetite. On the sixth day, or thereabouts, the forehead and face begin to grow rough as the pustules die off and as the skin breaks. Over the rest of the body the blotches are both very broad and very red. About the eighth day they disappear from the face and scarcely show on the rest of the body. On the ninth, there are none anywhere. On the face, however, and on the extremities—sometimes over the trunk—they peel off in thin, mealy squamulæ, at which time the fever, the difficulty of breathing, and the cough are aggravated"

Statistics.

Measles is a disease the mortality from which has been unaffected by the improvements recently effected in sanitation. This, which appears to be the universal experience, may be illustrated from the statistics of England and Wales, which will be quoted from the special report on the control of measles made by Dr. Theodore Thomson[1] to the Local Government Board, and published in the report of the medical officer for 1894–95. Measles has shown increasing mortality in England and Wales since the decade 1871–80, whereas the mortality of all the other principal diseases of the zymotic class, with the exception of diphtheria and whooping-cough, has decreased—in some instances very markedly—since that period. It is a zymotic disease highly dangerous to very young children, especially to those attacked by it in the second year of life. The annual mortality per one thousand of persons living at ages under five years was in the decennia stated, as follows:

1851–60.	1861–70.	1871–80.	1881–90.
2.8	3.0	2.57	3.13

The proportion of deaths produced by measles to the total population is considerably greater in towns than in country districts. Thus in the decennium 1881–90, the annual rates of mortality per one thousand living from the diseases mentioned were as follows:

	Measles.	Scarlet fever.	Diphtheria.	Whooping-cough.
England and Wales	0.44	0.33	0.16	0.45
Seventy-eight towns in England and Wales.	.59	.40	.17	.57
England and Wales exclusive of seventy-eight chief towns.	.33	.29	.16	.37

A curve showing the mortality from measles presents two maxima in each year, the one at the beginning of summer, the other in the early

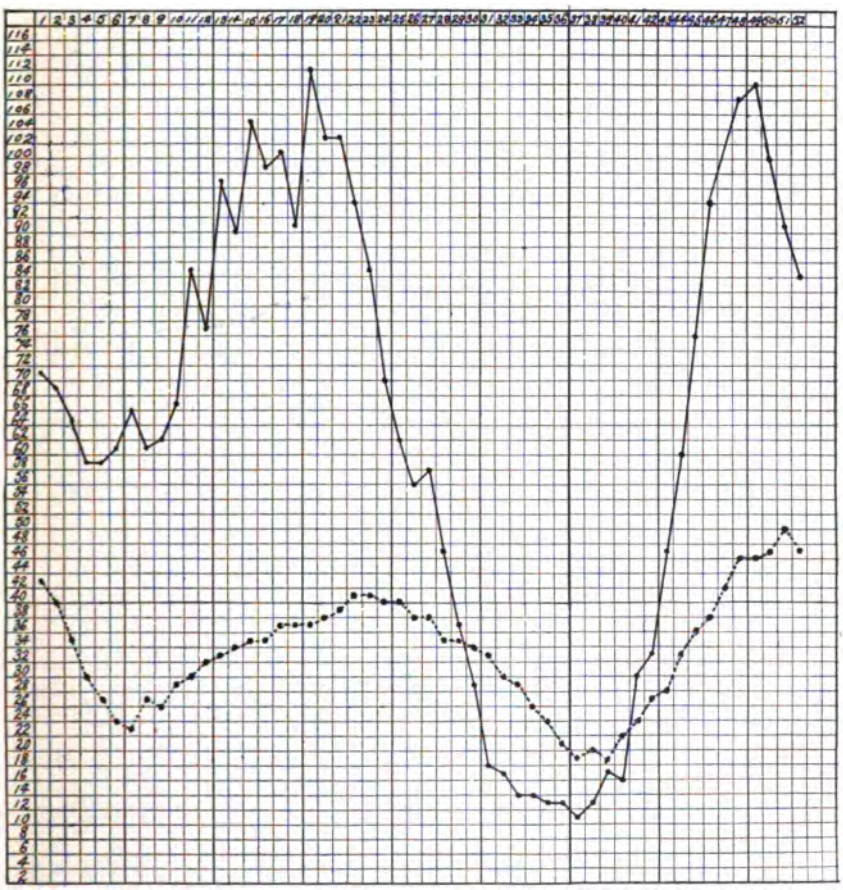

FIG. 4.—Curves Showing the Seasonal Variations in the Prevalence of Measles. The continuous line shows the weekly number of notifications in Budapest, the number being the average numbers for ten years, 1882-1891 (founded on Körösi's "Statistic der Infectiösen Erkrankungen," 1894). The broken line shows the weekly number of deaths in London; the number being averages of the numbers for fifty years, 1841-1890 (Registrar-General's Annual Summary, 1890). The fifty-third week, when it occurs, is in both curves ignored. In the Budapest curve the nearest whole number is taken. The figures in the column on the left indicate the number of cases or deaths; those in the horizontal column the weeks of the year in each set of statistics.

part of the winter. The mortality may be taken as a fair index of the prevalence of the disease, and the accompanying chart, in which the deaths from measles in London during a period of fifty years are contrasted with the number of notifications in Budapest for a period of ten years, illustrates and confirms this statement in an interesting manner.

Dr. B. A. Whitelegge,[3] in his Milroy lectures before the Royal College of Physicians on "Change of Type in Epidemic Disease," has examined the recurrence of periods of greater epidemic prevalence and has confirmed the results of other statisticians. The interval between these epidemic outbursts is generally about two years, but is sometimes six months more or six months less, due, Dr. Whitelegge suggests, to the fact of the seasonal curve showing two maxima. He believes also that there is distinct evidence of an epidemic wave of longer period, recurring at intervals of ten years, when a very high mortality is reached. He points out further that in populous places a series of epidemics may gradually raise the mortality of measles to a rate double or treble that of the ordinary seasonal maxima.

Observers in all countries agree in the statement that measles is much more fatal in the early years of childhood than subsequently. In the forty years, 1848-87, there were in England and Wales 367,602 deaths attributed to measles and 335,874 of these occurred among children of less than five years of age, leaving 31,728 only to be distributed among children aged five years and upwards. The distribution of these 335,874 deaths among children, aged under five, was as follows:

Under 1 year,	male,	3.01	deaths	per	1,000	living	at that age.
" 1 "	female,	2.51	"	"	1,000	"	"
1 to 2 years,	male,	5.81	"	"	1,000	"	"
1 " 2 "	female,	5.46	"	"	1,000	"	"
2 " 3 "	male,	2.88	"	"	1,000	"	"
2 " 3 "	female,	2.93	"	"	1,000	"	"
3 " 4 "	male,	1.60	"	"	1,000	"	"
3 " 4 "	female,	1.68	"	"	1,000	"	"
4 " 5 "	male,	0.93	"	"	1,000	"	"
4 " 5 "	female,	0.96	"	"	1,000	"	"

According to these data the age at which relatively the greatest number of children die of measles is the second year of life, while after the third year has passed there is a rapid decrease in the proportion of children dying of this disease. This large mortality is no doubt in part due to the far larger number of cases of measles which occur in children under five years of age; but this is not a complete explanation, for all statistics with which I am acquainted show that

the case-mortality of measles is very much higher under five years of age, and as a rule also show that the disease is particularly fatal to children in the second and third years of life. Thus Henoch, in his report on measles in the Charité Hospital in Berlin, from April, 1888, to October, 1890, records two hundred and ninety-four cases with eighty-nine deaths (thirty per cent.), distributed as follows:

	Cases.		Deaths.	Rate per cent.
1 year	59	133	74	55.6
2 years	74			
3 to 8 years	143	161	15	9.3
8 to 11 years	18			

Gannelon,[1] dealing with measles in the Hospice des Enfants Assistés in Paris for the five years 1887–91, gives the mean case-mortality of measles, cases complicated by diphtheria being excluded, as follows:

0 to 6 months,	23.68 per cent.	3 to 4 years,	13.66 per cent.
6 " 12 "	57.77 "	4 " 5 "	6.20 "
1 " 2 years,	53.94 "	10 " 20 "	nil.
2 " 3 "	27.73 "		

The rate of mortality shown in these statistics is extremely high and compares very unfavorably with that observed in private practice. But though the rate is much lower in private practice, the same special incidence on ages under five, and particularly in the second and third years of life, is apparent. This is illustrated by the following table extracted from one given by Dr. Theodore Thomson. It shows the number of persons at various ages attacked by measles in a certain town, during a period of about two years.

Age groups.	Estimated mean population, March, 1892, to March, 1894.	Attacks by measles March, 1892, to February, 1894.	Deaths from measles. March, 1892, to March, 1894.	Measles attack-rate annually per 1,000 living.	Measles death-rate annually per 1,000 living.		Measles fatality-rate per 1,000 attacked.	
0 to 1 year	1,155	166	16	72	6.9		96	
1 " 2 years	974*	233	46	119	23.6		197	
2 " 3 "	1,028	354	36	172	17.5	11.6	102	85
3 " 4 "	1,000	324	16	162	8.0		49	
4 " 5 "	951	324	5	170	2.6		15	
5 " 10 "	4,530	560	6	62	0.7		11	
10 and upwards.	25,968	39	0	0.75	0.0		0	
At all ages	35,606	2,031†	125	28	1.7		61	

* Based upon the 1891 census figures. No doubt there has been confusion at the census between children under one year of age and children over one year of age.

† As regards thirty-one of these persons there is no knowledge as to age.

It is probable that these figures show a case-mortality from measles which is rather above that usually met with in private practice, although this cannot be taken to be on the average much less than five per cent. In Edinburgh the number of deaths has varied from 1.5 to 5.9 per cent. of the cases notified. Hjort[8] in a local epidemic in Sweden which produced 228 cases (196 in children under fifteen years) observed 6 deaths (2.6 per cent.). Of these 4 were due to pneumonia and 2 to "croup."

The main cause of the mortality produced by measles is not the severity of the disease itself, which accounts for a comparatively small number of deaths, but the frequency with which certain complications occur. Of these the most fatal is bronchopneumonia. It is this complication which accounts for the enormous mortality which has been observed in asylums and other institutions. Membranous laryngitis, by which is to be understood as a rule diphtheria, is another complication which is responsible for a large number of deaths in hospitals and asylums.

Etiology.

Measles is in the vast majority of cases contracted by personal contact. It is very infectious during the primary period and probably equally so throughout the acute attack. A patient who has had measles can convey the infection after he is sufficiently convalescent to enable him to resume his usual occupation; but if disinfection has been resorted to, he is probably not liable to convey the infection beyond about three weeks after the appearance of the eruption. Infection persists longer, perhaps, in complicated cases and in those in which desquamation is well marked. Though the disease may be contracted from a convalescent whose illness began three weeks earlier, yet on the whole the infectious principle of measles possesses little resistance to external agencies and is little liable to be carried by fomites. It can, however, survive in fomites for a short time, and it is said to have been transmitted through the post. Though this occurrence cannot be altogether excluded, the infection certainly does not long remain attached to clothes or vessels. It is probable that the infectiousness of a patient is as great on the first day of the prodromal symptoms as at any subsequent date. The prodromal catarrh, moreover, may be very slight, and yet the infectious nature of the case may be very pronounced.

The notion that certain of the domestic animals may be susceptible to measles has been entertained by various writers on veterinary medicine, and it has even been asserted not only that sheep, pigs, and

dogs may suffer from the disease, but that all the domestic animals are liable to it. It has been suggested that under the head of "swine fever" are included certain cases which are due to infection with human measles. Behla,[9] of Luckau in Lausitz, Germany, has stated that he produced a disease resembling measles in a young pig by rubbing into the mucous membrane of the animal's nose, mouth, and throat the mucus from the nose and mouth of a case of measles in a child. Four days later the pigling had a discharge from the nose, and the eyes were red and watery. On the next day the animal was obviously ill, refused food, shivered, and had a temperature of 103° F. On the eighth day the muzzle, cheeks, and ears showed red spots, and twenty-four hours later the rash was general over the body. The most sceptical, we are told, would have admitted that the rash was like that of measles in the human subject. It was followed by slight desquamation. A fortnight later one of two adult pigs, which had, it was afterwards discovered, been in contact with the young pig for a short time, was taken ill, and the man in charge asserted that it was suffering from swine fever and would die. Examination of the blood and of the mucous secretions showed that the bacillus of swine fever was absent. In four days the pig began to get better, the rash disappeared, and was succeeded by slight desquamation. A week later the other pig began to be ill, and went through an attack similar to that experienced by the first pig, and to that from which the pigling had suffered.

Behla's experiment was repeated by Josias,[10] but with negative result. The latter, however, obtained positive results with certain monkeys experimented upon at the Trousseau Hospital in Paris.

Microparasites.—Although there can be little doubt that the infective agent of measles is a microparasite, no microbe has yet been certainly identified as the specific agent. In 1892 Canon and Pielicke described a short bacillus which they had found in the blood in cases of measles, which they thought might be identical with the "*bacilles très-courts*" previously found by Babes. They asserted that it differed essentially from the microorganisms described as occurring in the viscera, affected by the various complications of measles (p. 124). The bacilli were found during the whole course of the disease, but as a rule most abundantly at the time of defervescence, and disappeared early in convalescence. The bacillus could be cultivated in bouillon for one generation only. Bacilli of the same shape as those found in the blood were seen also in the expectoration and nasal and conjunctival mucus of children suffering from measles. Czajkowski has found a bacillus, apparently identical with that described by Canon and Pielicke, in the blood of a series of cases of measles. He was

able to cultivate it in nineteen cases in which he made the attempt; it grew not only in bouillon, as Canon and Pielicke stated, but also on glycerin-agar and on serum. On these solid media small colonies resembling minute rose-colored droplets formed in three or four days. It grew more freely when blood was added to the glycerinated agar. Bouillon and sterilized peritoneal fluid afforded the best media for the cultivation of the bacillus. It formed a white flocculent precipitate, which in old cultures acquired a yellowish tinge. In the blood the bacillus occurred usually singly, only rarely in groups, and was not evenly distributed. Grigorieff has also found this bacillus in the blood of thirteen cases in which he searched for it, and succeeded in cultivating it in bouillon in ten. Other observers have failed to confirm these results. Thus Barbier did not find the bacillus in the blood in any one of ten cases in which he searched for it, and Warschovsky also failed to find it in the twenty-one cases in which he searched for it.

Doehle,[35] in 1891, found certain bodies, which he believed to be protozoa, in the blood in eight cases. In the fresh blood he saw motile bodies both in the plasma and in the red corpuscles; shortly after the exanthem appeared the bodies were almost exclusively in the red cells. They measured from 0.5 to 1 μ, and presented an opaque nucleiform body surrounded by a clear zone. Later oval forms were seen containing two nucleiform bodies, and finally larger bodies (2 to 2.5 μ) containing several nucleiform bodies. Doehle's results have not been confirmed, but there are many who believe that the infective agent in measles, and probably also in smallpox and scarlet fever, will turn out to belong to the protozoa.

Pathology.

Skin and Mucous Membranes.—The eruption is produced by an acute congestion of the Malphigian layer, with infiltration of leucocytes around the vessels and glands; occasionally the red corpuscles escape also. The epithelial cells undergo a form of colloid degeneration. A similar process occurs in the mucous membranes, and the lymphatic follicles become distended by cells which invade the adjacent structures. The epidermal cells become swollen and detached, and this catarrhal inflammation may easily become complicated by ulceration which has its origin in destruction of the lymphatic follicles due to the intensity of the inflammatory process in them. The ulceration may then extend to the deeper parts, in the larynx for instance, to the cartilages. The lymphatic follicles and Peyer's patches of the intestine may show similar changes, and destruction

of the follicles may be followed by spreading inflammation which may even cause perforation (Worthington).

Lymphatic Glands.—There is some general enlargement and infiltration of the lymphatic glands in relation with the inflamed surfaces, but this is less marked than in scarlet fever. When there is much pharyngitis or stomatitis, especially if ulcerations have occurred, the cervical glands may undergo very considerable enlargement, and occasionally they suppurate.

Lungs.—The lesions of the bronchopneumonia present in so large a proportion of all fatal cases of measles do not differ from those of primary bronchopneumonia, but the process is perhaps more acute and the tendency to suppuration greater. In a considerable proportion of the cases in which death occurs with symptoms of bronchopneumonia, some weeks or months after the onset of measles, caseous pneumonia, a form of tuberculous infection of the lung, is found. Cornil and Babes have described under the name peripneumonia a form of inflammation of the lungs which they believe to be peculiar to measles and to be due to the direct action of the specific infection. It is an early complication and would appear to be the cause of death in those so-called "suffocative cases" to be presently described. The pneumonia is essentially interstitial, beginning in the lymphatic system and involving the interlobular and interalveolar tissue before determining a fibrinous effusion into the alveoli. These anatomical peculiarities indicate that the pneumonia is due to systemic infection. Taube has also observed the primary implication of the bronchial and pulmonary lymphatics accompanied by interstitial effusion.

Blood.—The changes in the blood are not very pronounced; there is no leucocytosis, but Demme found that during the febrile stage the number of red corpuscles was diminished to half, and that there were numerous microcytes and free nuclei. The proportion of fibrin to be obtained from the blood was diminished.

Symptoms.

Incubation.

The most usual interval between exposure to infection and the appearance of the eruption of measles is fourteen days, but it is not infrequently a day more or a day less; very rarely it may be as short as seven days. Intervals of sixteen, seventeen, and eighteen days probably occur occasionally, and their possibility should not be left out of consideration in reference to the question of the isolation of

susceptible persons who may have been exposed to infection. The primary, prodromal, or catarrhal stage may vary from one day to five days, and consequently the true incubation period of measles will be found by making a deduction from the periods mentioned above. The amount of this deduction cannot be laid down definitely, for there is no constant relation between the duration of the prodromal stage and that of the lapse of time between exposure to infection and the appearance of the rash. Usually the true incubation period of measles is nine or ten days, but it may be as long as fourteen or as short as five or even four days. A susceptible person must be observed for fully a fortnight after exposure to measles, and unless found free from fever and catarrh at the end of that time, it cannot then be asserted that the disease has not been contracted. During the period of incubation no departure from health is discoverable. W. Squire believed that there was a slight elevation of temperature about the sixth or seventh day of the incubation period, but I have never been able to detect any such rise of temperature, and Sevestre and Comby, who have also watched the temperature during the incubation period, have not noticed any departure from the normal.

Prodromal Stage.

The first symptoms of illness begin, as has been said, from eight to ten days after exposure to infection. Occasionally there is at the outset a slight rigor, or in young children convulsions, which, however, are usually slight and of short duration. As a rule the first symptoms resemble those produced by ordinary coryza, but the catarrh of the ocular, nasal, pharyngeal, and laryngeal mucous membranes is usually more intense. At this time the temperature is raised, and may be as high as 104° F. (40° C.). Cough begins early to be troublesome, but as auscultation seldom reveals any physical signs, beyond perhaps a few scattered sibilant râles, it is probably due to the condition of the fauces and larynx. The face is puffy, not usually flushed, but rather pale or a little dusky. The most characteristic symptom at this stage is photophobia which is often very pronounced, so that the child seeks out a dark corner or buries its head in the bedclothes or the cushion of a chair; the eyes water, the sclerotic is injected, and the palpebral conjunctiva is red and swollen. The nose discharges a thin watery fluid, which, owing to its irritating character, quickly leads to excoriation of the upper lip; the nasal discharge is often blood-stained, and in some epidemics epistaxis is observed in many cases and may be serious. The voice and cough are hoarse. This is due to laryngitis which may be severe enough, owing to œde-

matous swelling of the mucous membrane, to cause some dyspnœa, or may be complicated by laryngismus stridulus. The tongue begins to be covered with a whitish fur, but its edges remain red and there is enlargement of the papillæ. The mucous membranes of the mouth and pharynx are red and slightly œdematous. The swollen mucous membrane of the cheeks shows plainly the marks of the teeth, and the gums project around their necks. The surface of the mucous membrane is whitish and the epithelium may be detached in small flakes. During the course of the second day, in a large proportion of cases, the so-called enanthem appears on the palate in the form of numerous, closely set red points which run together into blotches and extend to the pharynx. The secretion from the nose and nasopharynx early becomes mucopurulent, and at about the same time (second day) the glands of the neck, especially those under the jaw, are found to be enlarged and tender. The patient exhales a peculiar fusty odor, rather like that of sour paste. The general malaise, the photophobia, and the thirst, by which it is continually tormented, render the child peevish and irritable. Cases are occasionally met with in which the patient during the prodromal stage remains in a dull somnolent state; such cases have been observed usually in epidemics. Wilischanin,* for example, observed this condition in every one of fifty cases in a girls' school, the ages of the patients varying from two to seventeen years.

Eruptive Stage.

On the morning of the third day there is usually some remission of the symptoms attended by a decline in the temperature, but on the evening of that day all the symptoms become aggravated. The temperature rises, the pulse becomes more rapid, the photophobia and catarrh are more intense, and the general discomfort and malaise more pronounced. The eruption is about to appear and already some faint red mottling may be noticed. It shows first on the forehead, generally at the edge of the hairy scalp or behind the ears, a little later around the eyes and mouth and on the chin and neck. The distribution is more or less symmetrical. The eruption, especially that on the face, is at first red and punctiform, or merely a diffuse redness of the skin, but in a few hours small, rounded red spots, which give the finger the sensation of soft papules very slightly elevated, form in the affected parts. They are scattered irregularly and as they enlarge form patches often crescentic in form, with a scalloped edge. The skin between appears healthy, and the color of the spots is at first discharged by gentle pressure with the finger. Later the red of the

spots becomes tinted with purple, and they do not disappear on pressure.

The eruption usually spreads in an orderly manner downwards from the face, reaching the trunk and the upper limbs on the second day and the lower limbs on the third. The eruption in any particular region begins to decline in about twenty-four hours, so that it is fading on the face, while it has not come fully out on the lower limbs. Occasionally there may be distinct intervals so that the eruption appears in crops. Its appearance on the lower part of the body may thus seem to be a second eruption; such occurrences are sometimes improperly spoken of as relapses. In other cases again the eruption comes out at first in a characteristic manner on the face and neck, but then fades rapidly without extending to other parts. This failure to spread, if accompanied by a decline of temperature towards the normal and general amelioration in the symptoms, indicates a mild attack; on the other hand, a similar arrest of the eruption may be associated with the onset of some of the serious affections of the internal organs which will be mentioned below under complications. The eruption on the trunk and limbs is generally most copious at the flexures of the joints, or at other natural folds, and at points where the skin is pressed upon or chafed by clothes.

While the eruption is coming out the catarrh of the mucous membrane increases; the conjunctivæ are red and swollen, the eyes water freely, and photophobia is intense; the discharge from the nose becomes purulent and is excessively irritating to the nostrils and upper lip. The aggravation of the laryngeal catarrh is indicated by hoarse voice and cough and frequently by a little inspiratory stridor. If a laryngoscopic examination is made at this stage, the laryngeal mucous membrane is seen to be much congested, and even the vocal cords may be slightly reddened.

The eruption may depart from the type in character, intensity, and distribution. Occasionally it appears as early as the second or even the first day of fever and coryza. It may be delayed until the fifth or sixth day, and when there is a remission on the third day it may be erroneously assumed that the child had simple coryza. When the cutaneous congestion is greater than usual, the rash may have a papular appearance. In cachectic children the rash is commonly discrete and pale, but sometimes its general appearance is much modified by ecchymoses which are most often seen and are most extensive on the back and thighs. In children infested by fleas or lice, the general tint of the rash may be deepened by the existence of very numerous petechiæ. Occasionally on the abdomen and thighs a miliary eruption is mixed with the true measles eruption. In infants,

especially in rickety infants, and in warm weather, the true eruption is often preceded by sudamina. The eruption at its first appearance, especially if this occur rather earlier than usual, may produce an almost uniform reddening of considerable areas, and thus resemble the rash of scarlet fever, so that it may be supposed that the child is suffering from that disease, or from both diseases. The eruption, even when confluent, will usually have a scalloped and well-defined edge. However, the diagnosis will ordinarily be placed beyond doubt in a few hours.

Signs of bronchitis are seldom absent at this stage. Rhonchi at first sibilant, later sonorous and hurried, may generally be heard in all parts of the chest, but are most numerous in the interscapular region and seldom absent there. Young children as a rule do not expectorate, but at a more advanced age the expectoration is at first clear and stringy, but becomes purulent and nummular; at both stages it is remarkably viscous and tenacious. The child continues to be extremely thirsty, but refuses food. Diarrhœa of foul-odored, slimy stools very commonly occurs during the eruptive stage, either at the onset of the eruption or as it fades. At night the patient is restless and peevish, but is more tranquil by day, much of which is often spent in sleep. The eruptive stage lasts four or five days, but may extend to six days.

Convalescent Stage.

As the rash fades the general symptoms improve, the thirst diminishes, the nasal discharge decreases, sleep becomes natural, and appetite returns. Cough and other signs of bronchitis, as well as some dislike of light persist for a few days more, but at the end of ten days or a fortnight from the onset of the prodromal symptoms the patient will be apparently quite well. A small amount of desquamation may generally be observed, especially about the face, neck, and waist, after the disappearance of the eruption. It is fine and branny, except when there has been a miliary eruption. After a miliary eruption the scales may be much larger than usual.

Temperature.

Both the height to which the temperature attains and the form of the curve vary a good deal in individual cases. As a rule it is possible to distinguish a double summit to the curves, a sharp rise to 103°, 104°, or even 105° F. (39.4°, 40°, 40.5° C.), at the onset of the prodromal symptoms, followed by a somewhat rapid fall which lasts about twenty-four hours and often reaches the normal line or even

falls below it. To this succeeds at the end of the second or beginning of the third day a rise, at first gradual, and then, as the eruption appears, more rapid. The maximum, 104° to 105° F., is usually attained at this moment, and a more or less marked remission occurs, followed by one or more elevations as the eruption continues to come out. These occur usually in the evenings, and the maximum for the attack may be attained on any one of these occasions. If there be no complications the temperature begins to fall as soon as the eruption ceases to come out. The fall though rapid is gradual and occupies twenty-four or thirty-six hours. The accompanying chart (Fig. 5)

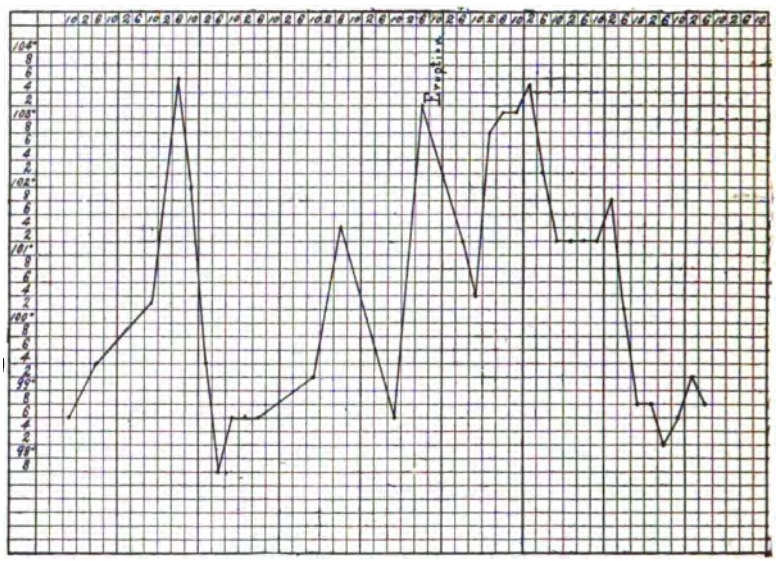

FIG. 5.—Temperature Chart in a Case of Measles of Average Severity without Complication.

of the temperature in a case of measles in which the attack was of average severity but uncomplicated, exhibits fairly well the typical characters of the curve, and in particular the fall after the initial rise (prodromal stage) which in this case extended below the normal. Within a week of the appearance of the eruption the child was quite well.

The following temperature chart (Fig. 6) for which, as well as for the next, I am indebted to Dr. R. P. Cockburn, resident medical officer of the East London Hospital for Children, Shadwell, is an example of the course of the temperature in a very mild attack of measles in a child previously in good health. The prodromal symptoms were very slight—slight bronchitis with little or no coryza. The eruption came out very rapidly and was well developed, but the erup-

tive stage was short and the general symptoms slight; "the child never looked ill."

Only very rarely is there a distinct crisis with profuse sweating and sudden fall of temperature. Such a crisis may be attended by collapse. In some cases there are regular morning remissions and evening exacerbations of the temperature during the prodromal stage; in others the initial rise at the onset of the prodromal symptoms is not well marked, but the temperature mounts gradually to 100° or 101° F., and remains at about that level until, with the appearance of

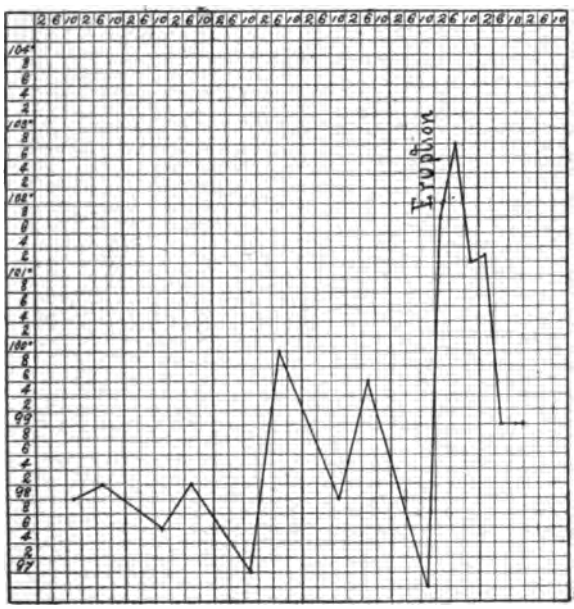

FIG. 6.—Temperature Chart in a Mild Case of Measles.

the eruption, it rises rapidly to 103° or 104° F. When the case is complicated, defervescence may be much delayed. The form of the temperature curve will depend on the nature of the complication.

The next chart (Fig. 7) shows the course of the temperature in a boy, aged nearly three years, who had recently recovered from an attack of bronchopneumonia. He was then probably already suffering from tuberculosis in a chronic form. The prodromal stage was prolonged, lasting fully six days. During the eruptive stage there was extensive bronchopneumonia and the child was very ill. The temperature fell when the eruption faded, but immediately rose again. The bronchopneumonia did not clear up and the child died just four

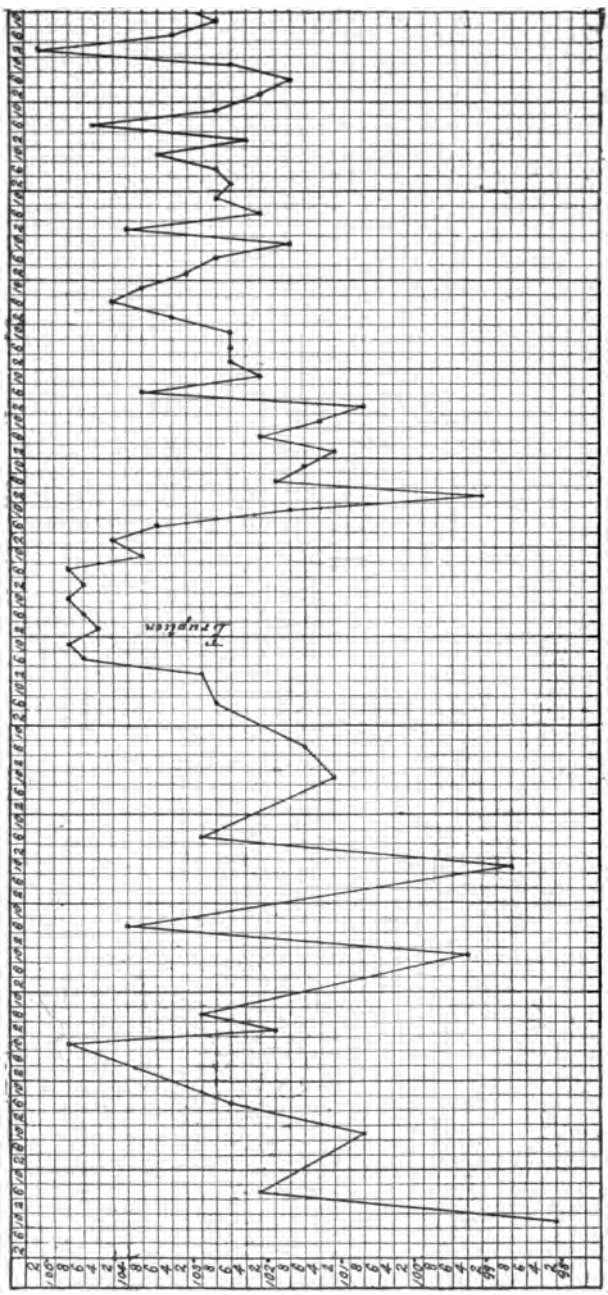

FIG. 7.—Temperature Chart in a Case of Measles Complicated with Bronchopneumonia.

weeks after the commencement of the prodromal symptoms. Post-mortem examination showed extensive caseous bronchopneumonia and general tuberculosis.

Hyperpyrexia is rare; it occurs usually at about the time of the first appearance of the eruption, but may be delayed until the second or third or even the fourth or fifth day of the eruption. It is attended by extreme depression, loss of consciousness, cyanosis, and disappearance of the eruption, irregular breathing, and rapid pulse. Temperatures of 108° and 109° F. (42.2° and 42.8° C.) have been noted and there appears to be no record of the recovery of any patient in whom even the lower of these two temperatures was reached.

Departures from the Usual Course.

Prodromal Stage.—The prodromal stage may be very short, as already mentioned, or it may be prolonged to six or even eight days. Not infrequently symptoms during this stage are so slight that they pass unobserved.

Abortive Cases.—Sometimes, as already said, the disease appears to abort early in the eruptive stage, and convalescence begins on or about the second day.

Measles without Eruption.—Occasionally the disease runs its course, but no eruption appears. In a recent epidemic at Heidelberg Emb-den' saw twenty cases of this kind. They can be diagnosed only when they occur during an epidemic. The symptoms, fever, catarrh, bronchitis, and gastric derangement resemble those of influenza, but the patient is found not to contract measles if exposed subsequently to the infection.

Malignant Forms.—Though as a rule benign, measles may be a most severe disease, owing either (*a*) to the intensity of the affection, or (*b*) to the cachectic condition of the individual attacked. Severe epidemics have occurred chiefly in communities not previously affected (Faroë Islands, Fiji), or in crowded institutions. Severe cases may be met with in any epidemic, and appear often to be traceable to insanitary surroundings which increase the liability to complications, while their continuous influence has probably already deteriorated the patient's health.

Typhoid Form.—The eruption does not come out well, or if it has begun to appear in the ordinary way its progress is checked and the spots fade. The statement often made that this retrocession of the eruption is the cause of the severe course which the disease subsequently follows, expresses a view which is probably erroneous. The condition of the patient generally soon becomes alarming. The pulse is increased in frequency to 130 or 140, the respirations to 60 or 80, the temperature rises to 104°–105° F., the tongue becomes dry, the lips cracked, the skin burning, and the excretion of urine is much diminished. In young children the change for the worse commonly begins with convulsions which are repeated again and again; older patients become delirious. The delirium may be violent at first, but whether the onset be marked by convulsions or delirium the patient quickly becomes prostrate and finally passes into a comatose state. In the most severe cases this stage is reached in a few hours. In others, after an attack of convulsions or after delirium attended by dry tongue, hot skin, and rapid pulse and breathing has lasted for some hours,

the symptoms rapidly improve and the case runs an ordinary course. Every degree of severity between these two extremes may be observed (see the section on complications, "Septicæmia").

Suffocative Form.—Cases now and then occur, generally in epidemics in schools or barracks, in which at about the time of onset of the eruption the patient is seized with severe dyspnœa and becomes cyanosed. Cough is frequent, and the patient, if old enough, expectorates a frothy mucus. At first the physical signs are not definite, but a little later fine mucous râles are heard everywhere in the chest and the patient succumbs to what is called capillary bronchitis. In the adult death may be determined by syncope; in children by a more gradual failure of the heart. The eruption is scanty, or if it has appeared freely it fades at the onset of the dyspnœa. Apparently these cases are examples, in its most acute form and earliest stage, of the peculiar specific infection of the lungs described by Cornil and Babes.

Hemorrhagic Form.—As already said, hemorrhages may occur into the eruption, especially in cachectic children, and epistaxis is not very uncommon, especially in some epidemics, and does not appear seriously to aggravate the prognosis. But a form of measles is described, especially by the older writers, in which the disease is very severe and its symptoms are adynamic from the onset. Hemorrhages take place into the skin before the eruption comes out, or into the eruption if it has already appeared, so that it has a purpuric aspect. Blood is discharged from the nose, the bowels, and the vulva. The urine also may contain blood, and extravasations may take place into the viscera. Cases of this character are seldom or never seen at the present day, and as Fagge[8] has said, "when one finds the older writers laying great stress upon 'black measles,' one is almost inclined to suspect them of having mistaken cases of hemorrhagic smallpox for this disease; and it is interesting to notice that Sydenham speaks of an unusually bad kind of measles as prevailing in London in 1670 and 1674, at a time when variola also was remarkably malignant and fatal."

"*Secondary*" *Measles.*—If a patient whose health is enfeebled by a recent attack of typhoid fever or diphtheria, or by tuberculosis or malnutrition, contracts measles, the disease is apt to run a severe course. The febrile reaction characteristic of the prodromal stage is not well marked, the eruption is scanty, dusky, or purpuric, the temperature is continuously high, and vomiting and diarrhœa are common. In young children bronchopneumonia nearly always supervenes and the mortality is high. On the other hand, ill-nourished children sometimes have measles in a very mild form if their general surroundings at the time are good, and if they can be well nursed in properly ventilated rooms.

Relapse.—Although a different opinion has sometimes been expressed, there can be little doubt that relapse is an extremely rare event. Many of the instances quoted are to be accounted for by an error of diagnosis. The first illness diagnosed as measles has been rubeola (rötheln) or scarlet fever, or a simple roseola. Or after a true attack of measles, the eruption of scarlet fever or rubeola or a drug rash may be the source of error. In other cases quoted as instances of relapse, there would appear to have been no more than a temporary retrocession of the eruption or an unusually long interval between its appearances on different parts of the person. A few instances, however, remain in which the eruption attended by the usual symptoms has reappeared some days or weeks after its disappearance in the ordinary course.

Second Attacks.

There is a widespread popular belief that second attacks of measles are very common. This belief is, however, undoubtedly erroneous and rests upon errors of diagnosis, an attack of rubella or an outbreak of roseola or of general dermatitis being mistaken for measles. Such mistakes are the more likely to arise, as medical advice is often not sought in mild attacks of rubella. Senator[9] has recorded five instances of second attacks, yet expresses the opinion that such occurrences are rare, far more rare than in scarlet fever. Embden[7] met with five second attacks during the course of a single epidemic, but not a few of the cases recorded as examples of second attacks ought perhaps more properly to be called relapses, as, for example, the case reported by Streng,[10] in which the second eruption appeared only eight days after the first and only two after the temperature had fallen. Henoch,[11] while recording a single case which came under his own observation, expresses the opinion that second attacks are exceptional. The evidence from epidemiology shows pretty conclusively that a second attack of measles is very rare. Thus Panum states that during the epidemic on the Faroë Islands in 1846, all the old people who had the disease in the epidemic of 1781 escaped, while nearly all the other inhabitants suffered. Hardaway[12] quotes from Woodward the observation that during the American Civil War members of regiments drawn from rural districts who had not had measles took it in large numbers when exposed to the infection, while the regiments drawn from urban districts escaped. Some of the few cases of second attacks recorded lend some support to the theory that the immunity acquired during the first attack has been imperfect, owing to some peculiar localization of the specific processes then.

Thus Gottstein reports the case of a girl, aged ten years, who had an attack of measles which was marked by abundant eruption, but attended by very slight affection of the respiratory and conjunctival mucous membranes. Two years later she had a second attack in which the prodromal symptoms (fever, angina, bronchitis, conjunctivitis, and coryza) were extremely violent, while the eruption was delayed and little marked. He argues that, judging from the symptoms, the virus seemed to act in the first case especially upon the skin and only slightly upon the mucous membranes. Such speculations are perhaps a little fanciful, and the fact remains that practically one attack of measles confers immunity for life.

Complications.

Larynx and Pharynx.

Some degree of *catarrhal laryngitis* is so commonly observed that it ought to be reckoned rather as a symptom than as a complication of measles. It passes away usually about the time the rash appears or at least does not endure beyond it. It may determine one or more attacks of laryngismus stridulus, which occur commonly at the onset of the disease but may be noticed even as late as the convalescent stage. The voice and cough are hoarse and in many cases the respiration is not quite clear in the intervals, and there is some recession of the lower part of the sternum and at the epigastrium. It is, however, occasionally so intense that intubation has become necessary. In other cases ulceration occurs or the larynx becomes the seat of false membranes.

Ulcerative Laryngitis.—The symptoms of laryngitis instead of clearing away become more marked, the voice grows more hoarse and finally toneless, cough excites acute pain, referred to the larynx which is tender on pressure, and the expectoration if present is blood-stained. Death may be brought about by the rapid development of œdema glottidis; necrosis of the cartilages of the larynx may occur and gangrene has been described. Even mild cases are very apt to be followed by hoarseness, which is often long-lasting and sometimes permanent, owing to partial destruction of the vocal cords.

Membranous laryngitis is a very fatal complication of measles. It is rare in private practice but has prevailed in certain epidemics in schools and asylums, owing apparently to overcrowding and other insanitary conditions existing in these institutions. In the Hospice des Enfants Assistés in Paris[4] this complication was observed 235 times in 1,633 cases of measles. Of these 235 cases no less than 218

succumbed, whereas among the remaining 1,398 cases of measles only 388 died. It may appear during the eruption or after it has faded—from the third or fourth day to the end of the second week. This membranous laryngitis is due in some cases to infection with true diphtheria; in others, perhaps the majority, it is due to infection with pyogenic cocci. The symptoms are practically identical, but the membrane produced by the infection with the pyogenic cocci is less dry and coherent, more diffluent or friable than that produced by diphtheria. The false membrane may not be limited to the larynx, but may invade the fauces and tonsils, the mouth, lips, and nasal passages. The symptoms referable to the larynx may come on suddenly, but as a rule the onset is more insidious than in primary diphtheria; attacks of dyspnœa are less frequent and there is altogether less warning of the approach of asphyxia. When once symptoms of asphyxia become distinct, death is not far off. Tracheotomy is of little avail, for the lungs are almost certainly already the seat of extensive bronchopneumonia, and the membrane has in many cases invaded the trachea and bronchi. Even in those cases in which tracheotomy is followed by some improvement in the general condition, the prognosis is still very bad, and the wound itself is very apt to become the starting-point of extensive phlegmonous inflammation, of erysipelas, or of gangrene.

It must be confessed that the diagnosis from the clinical appearances between these two forms of laryngitis (ulcerative and membranous) is often impossible, unless the membrane extends to the pharynx or fauces. Satisfactory laryngoscopic examination is very difficult in those cases in young children in which the information it would afford would be most valuable. Bacteriological examination will assist in the identification of those cases which are due to true diphtherial infection.

Otitis.

Otitis is an exceedingly common complication of measles. Indeed some writers have held that an inflammatory affection of the middle ear was part of every case of measles. This view was put forward by Tobeitz, and has been supported recently by Bezold,[14] whose conclusions are based upon the exploration of the ear in a large number of cases, and upon the post-mortem examination of sixteen fatal cases. Examination of the middle ear in the sixteen cases revealed evidence of otitis media. Effusion, sometimes mucopurulent, but in other instances purulent, was found in the tympanic cavity, in the antrum, and in the mastoid cells when these were sufficiently developed. In one case only did these parts escape and in this effusion was present

in the osseous part of the Eustachian canal. The mucous membrane of the parts mentioned was congested, and exhibited a network of small vessels and in some cases minute hemorrhages. Bacteriological examination showed that the microbes present were either streptococci (in about half the cases) or staphylococci (white or orange). The same organisms were found with the same relative frequency in fluid obtained by puncture of the tympanum during life. Bezold agrees with Tobeitz in believing that this form of otitis begins very early in the course of the disease, probably as early as the eruption, and that it is fully developed on the fourth day of the eruption. He holds that it is analogous to the erythematous condition of the mucous membrane of the mouth and eyes. He does not believe that it is due to infection from the nasopharynx as in the more severe form of otitis which occurs somewhat later in the disease. This is shown by the fact that the cartilaginous part of the Eustachian tube is not involved. He argues further that the constancy of its occurrence proves that it is due simply to a localization of the virus in the mucous membrane, which produces an inflammatory condition, which again, according to a well-known law, permits and encourages the development of the pyococci. It is a comparatively mild affection, which does not produce distinct symptoms as a rule, and seldom leads to perforation. When this does occur cicatrization is complete, and there is a perfect *restitutio ad integrum*. Bezold confirms this conclusion from his clinical observation of cases of measles by a record of an examination of a number of school children who had and had not had measles, and in whom no difference could be detected in the state of the drum.

Otitis, however, may under certain circumstances of not infrequent occurrence be a most serious complication of measles. This form of otitis media is important from two points of view. It may be the cause of death, or at least of very great suffering, during the attack of measles, and if the patient recovers it may determine chronic middle-ear disease with all its serious disabilities. The Eustachian tube becomes involved by extension of inflammation from the fauces and pharynx. The walls of the tube become swollen and its lumen is thus diminished. If the swelling be sufficiently intense, the tubes may be entirely closed, and the morbid secretions are thus penned up within the cavity of the middle ear. Short of this the tubes may be blocked, perhaps only at their orifices, by inspissated mucus. In cases of the latter class the child may suddenly be seized with pain, which, if old enough, he refers to the region of the ear. Relief may be obtained after a few hours of suffering, owing to the plug of mucus having been expelled into the pharynx. On the other hand, when

inflammation is more intense and the blocking more complete, the increasing tension in the tympanum, produced by the accumulation of the secretions, gives rise to symptoms which are liable to be mistaken for meningitis. In measles this inflammation is apt to be rapid and intense, and early assumes the suppurative form. But as Dr. Walker Downie[15] has pointed out in an excellent paper on the care of the ear during the course of the exanthemata, there are other causes at work. Severe affections of the ear in measles are met with most often in children who have previously suffered from faucial and pharyngeal catarrh and adenoid vegetations. Such children are always dangerously open to Eustachian catarrh and inflammation of the middle ear; but while they are able to run about, occupying for many hours out of the twenty-four an upright position, the increased pharyngeal secretion is prevented from collecting to any extent within the nasopharynx. If after such a child is attacked by measles it is at once confined to bed, the quantity as well as the infective nature of the secretions is much increased. In the horizontal position the secretions from the nose and from the pharynx are retained above and behind the palate, and the direction which the Eustachian tubes then have interferes with the escape of inflammatory products from the middle ear. Failing to find ready exit, the mucous secretions quickly become purulent, the lining membrane of the tympanum becomes necrosed, the bony cells communicating with the tympanum are filled with the products of suppuration, and extensive necrosis, or even gangrene, may occur. Dr. Walker Downie's statistics show the importance of measles as a cause of chronic disease of the middle ear. Of 501 consecutive cases of tympanic involvement seen among children varying in age from seven weeks to twelve years, at the Dispensary of the Royal Hospital for Sick Children in Glasgow, the disease originated during an attack of measles in 131 cases, or 26.1 per cent., while the number which arose during an attack of scarlet fever was only 63, or 12.6 per cent.

The recognition of the occurrence of this complication coming on during the course of a severe attack of measles often presents considerable difficulty, especially if the patient is too young to locate the seat of pain, or if, either on account of the severity of the attack of measles or, as is sometimes the case, of the sudden onset of stupor or delirium due to the tympanic involvement, the patient is unable to indicate the seat of the pain. As a rule, however, it is not difficult to perceive that the patient is suffering from pain, his discomfort being indicated by a constant whining, by sudden screaming fits, great restlessness, and perhaps tossing of the head. The complication is most apt to arise about the end of the second week, with

symptoms such as those indicated above, and even in their absence persistent elevation of temperature without other discoverable complication should lead to at least a suspicion that the ear is involved. Examination of the tympanum will show the signs of inflammation, redness, and loss of lustre, with (if suppuration has already occurred, as may be the case in an early stage) a yellow discoloration in the lower segment. In infants, owing to the smallness of the parts and the oblique position of the tympanum, the examination is very difficult and the diagnosis must often be largely conjectural. The symptoms bear a close resemblance to those of meningitis, with which indeed the tympanic inflammation is very apt to become associated. Not only may the suppurative inflammation extend to the mastoid antrum or the mastoid cells, but by continuity of substance may reach the meninges of the base, or actually perforate the roof of the tympanum, or, as Ashby and Wright have pointed out, find its way through the sutura petromastoidea, which is still open in infancy. Extensive suppurative meningitis may ensue, or cerebral abscess, or the lateral sinus may become thrombosed, and pyæmia result. Another possible complication is that the carotid artery may be opened by ulceration, and hemorrhage—which will probably be fatal—ensue. Occasionally the inflammation reaches the temporomaxillary joint, producing arthritis, and perhaps a permanent stiffness of that joint.

Deaf-Mutism.

A considerable proportion of the cases of deaf-mutism in Great Britain, America, and the continent of Europe date the loss of hearing from an attack of measles. In most of the cases secondary to measles, if not in all, the deafness is due to disease of the internal ear which has been propagated from the middle ear. According to statistics collected from institutions for the education of deaf-mutes in Great Britain, by Kerr Love and Addison,[14] of 1,410 deaf-mutes 138 attributed their loss of hearing to damage done during an attack of measles. This is nearly 9.8 per cent. Among 1,673 acquired cases in American institutions there were 52 in which the deafness was attributed to measles (3.1 per cent.), and among 1,989 in continental institutions, 84 were due to measles (4.2 per cent.). This discrepancy is to be accounted for partly by the peculiar liability of epidemic cerebrospinal meningitis to produce deafness, for this epidemic disease is extremely rare in Great Britain. Omitting the cases attributed to this disease in the American and Continental statistics, we find proportions due to measles of 3.8 per cent. and 5 per cent. respectively. It would appear, therefore, that measles does produce more

cases of deaf-mutes in Great Britain than in the rest of Europe or in America.

In the majority of cases of deafness produced by measles the inflammatory process has extended from the nasopharynx to the middle ear, and only after disorganizing that cavity extends to the internal ear. Of the lesions of the middle ear which otitis media may produce, those which are of most importance in this connection are sclerosis and ossification of the fenestræ, since these apertures enter into the wall of the labyrinth. Similar changes may occur in the tympanic membrane, producing alterations in its curve, loss of lustre, and thickening of its structures, with perhaps calcareous deposits and eventually ossification. In a minority of cases the structures of the internal ear are disorganized without the persistence of any marked changes in the middle ear to be discovered during life. Thus Kerr-Love found the tympanic membrane perfectly normal in four out of ten cases of deaf-mutism due to measles.

The nature of the changes in the internal ear are not in all cases the same in extent, but they are always of the nature of sclerosis, and destruction of the membranous labyrinth. The cochlea may be encumbered or closed by bony growths, and the osseous lamina distorted and its structure converted into fibrous tissue.

With regard to the character of the pathological process in the internal ear which brings about these changes, a case reported by Moos[11] may be quoted. The patient, a boy aged three years, developed an affection of the labyrinth during the course of an attack of measles. He died and at the post-mortem examination, in addition to the changes in the middle ear proper, there was a perforation in the membrane which closes the fenestra rotunda, while inflammatory signs were present in its neighborhood. Ossification had begun in the cochlea, although the disease process was not more than a fortnight old. Thrombosis and degenerative changes were also going on. The changes are traced by Moos to bacterial invasion.

Mygind[18] gives a case examined at a later date, in which it was found that the disease had spread from the nasopharynx to the middle ear, and thence to the mastoid and internal ear. The membranous contents of the labyrinth had disappeared, the right mastoid was sclerotic, and the tympanic membrane thickened and calcareous; the left membrane was completely destroyed and the tympanic cavity was filled with gelatinous matter.

The Lungs.

Pulmonary affections are the most frequent complications of measles and are the principal cause of the great mortality produced by the disease. A certain amount of *bronchial catarrh* is so generally observed that it must be considered to be a symptom rather than a complication. The smaller bronchi and the pulmonary tissue proper may become involved in the inflammatory process at any stage of the disease, and as the nature and clinical characters of the affection vary at the several stages, it will be convenient to follow the order of time.

During the prodromal stage signs suggesting *capillary bronchitis* may develop rapidly. The respiration is hurried (20 to 50), there is a short troublesome cough, slight cyanosis; the pulse is rapid and soft, and everywhere over the chest small crepitations are heard. Resonance is not deficient anywhere, expansion is good and equal, the breath sounds are not tubular or even bronchial, and the true fine crepitation at the end of inspiration so characteristic of early pneumonia is not heard. As a rule this condition, to which the term "congestion of the lungs" is very commonly applied, does not last long, but disappears usually at or soon after the time of appearance of the rash. Occasionally, however, the symptoms persist and the physical signs of pneumonia develop. These cases, it is probable, correspond with the true measles pneumonia of Cornil and Babes'[1] mentioned above; in other instances persistence of the pulmonary signs indicates the lighting up of a tuberculous process. Indeed, if physical signs of capillary bronchitis or pneumonia which have been discovered during the prodromal stage continue through the stage of eruption, a guarded prognosis should be given even though the temperature be not very high and the general condition improve, as the rash, which is often not well developed, disappears, for in many such cases the health is not reëstablished and the patient ultimately develops tuberculosis.

Bronchopneumonia is most often met with during the eruptive stage, and it is the form of pneumonia which determines the largest number of deaths. This bronchopneumonia as a rule develops at about the same time as the eruption, but it may come on a few days later and even when convalescence seems to be about to commence. The onset of the bronchopneumonia is indicated by increased rapidity of respiration, already somewhat hurried owing to the bronchial catarrh. The respiration is not only hurried but labored, the patient suffers much from the oppression of breathing and seeks relief by sit-

ting up; the nostrils expand with inspiration, the accessory muscles of respiration are called into play, the face is dusky, and altogether the dyspnœa observed in the bronchopneumonia of measles is greater than that produced by an attack of primary bronchopneumonia involving a similar extent of lung. The physical signs are at first rhonchi and subcrepitant râles disseminated widely through the lungs, but after a day or two, signs of distinct pneumonia—deficient resonance, bronchial breathing, and fine crepitations—are found in one or both lungs, most commonly first in the interscapular regions but not infrequently at the apex. Occasionally the extent of lung involved appears to be very great, and the patient succumbs to so-called "suffocative bronchitis" on the second or third day of the complication. A rare termination of bronchopneumonia in its most acute form is gangrene of a portion of the lung.

This bronchopneumonia, which is observed so commonly and is so frequently the cause of a fatal ending in measles, is to be attributed to a secondary infection. It occurs with great frequency in schools, orphanages, and hospitals, in the crowded dwellings inhabited by the poorer classes in towns, and generally under any circumstances which compel an accumulation of susceptible children, especially in old or dirty buildings.

Various microorganisms are found in the lungs in these cases, but the pneumococcus, the streptococcus pyogenes, and the staphylococcus pyogenes aureus are most often met with. All the microbes may be found in the secretions of the mouth, nose, and larger bronchi even in health, but are present in these situations more constantly in children suffering from measles. The catarrh determined by the primary infection of measles appears to favor the growth of the microbes mentioned, and by their agency the catarrh is intensified and spread.

As the eruption subsides, or even later when convalescence has commenced, the patient may begin to suffer from irregular pyrexia characterized by evening exacerbations and accompanied by cough and signs of localized pneumonia. This is the subacute or chronic pneumonia of measles, and is very often an indication of the commencement of a tuberculous process. In such cases bronchopneumonia has generally been present during the exanthematous stage, and the form of pulmonary tuberculosis which ensues is that commonly known as cheesy (caseous) pneumonia.

Pleurisy with effusion is a very rare complication or sequela of measles. In some cases at least it would appear to be secondary to follicular enteritis (see below).

The Gastrointestinal System.

Stomatitis.—Some general catarrhal inflammation of the buccal mucous membrane appears to be an invariable accompaniment of an attack of measles. It comes on during the prodromal stage and passes away with the eruption. There is a general swelling of the mucous membrane of the gums, cheeks, tongue, and palate; the color is purplish red at first, but the heaping together of epithelium combined with some œdema of the submucous tissue may produce an appearance which may be mistaken for false membrane, especially on that part of the mucous membrane of the cheek which corresponds with the interval between the upper and lower molar teeth. After a time, indeed, a soft, whitish, opalescent, or creamy layer forms which may be easily detached with the tip of the finger. This condition, in which catarrh predominates, is sometimes spoken of as an enanthem. It is chiefly of importance because it paves the way for secondary infections; of these the most serious is diphtheria, but pyogenic infections are much more frequent and are capable of causing much discomfort, of retarding recovery, and even of endangering life. Aphthous stomatitis may also be met with. Ulcerative (or impetiginous) stomatitis attacks particularly the sulcus between the lips, especially the lower lip and the gums. Small, round, or oval white patches form in the first place, and the necrosed epithelium is then detached, leaving a shallow ulcer with sharp or ragged edges. These ulcers may by extension unite to form large elongated ulcerated areas, with a purulent sloughy surface. They bleed easily, and this is especially noticeable when the outer border of the lips is involved; this becomes covered with crusts of clotted blood under which suppuration proceeds rapidly, and is often fissured in various directions; every movement of the lips is painful and the child refuses food and even drink. The staphylococcus pyogenes aureus has been found under this circumstance almost pure. The ulcerations tend to heal as the fever subsides, but if neglected, and especially in cachectic children, they may persist for long periods and be productive of much suffering.

Diarrhœa.—Some looseness of the bowels is the rule during the preëruptive period. An attack of diarrhœa is not uncommon at or about the period when the eruption is coming out; the stools are loose, watery, or glairy, showing probably that the whole extent of the intestine is affected by catarrh, and often foul-smelling. Occasionally this early diarrhœa is very copious, and the child becomes collapsed as in summer diarrhœa. To this form the term choleriform is ap-

plied, and as the eruption is ill-developed if the diarrhœa have commenced before its appearance, or fades when collapse commences, mistakes have been made and the diarrhœa of measles has been attributed to an attack of cholera infantum. There is also a dysenteric form of diarrhœa which is occasionally observed as a late complication of measles. It comes on when the rash is fading or even after convalescence appears to have been established, and may occur in cases in which there has been no diarrhœa during the early stage. More rarely it begins during the prodromal stage, and continues throughout the whole attack. After in most cases suffering from colic for some hours the patient begins to pass stools containing much mucus at frequent intervals. The motions are sometimes blood-stained and contain pus. The lesions found after death are those of more or less intense enterocolitis, most severe in the lower parts of the large intestine; in the most severe cases the sigmoid flexure and the rectum present ulcerations precisely similar to those seen in true dysentery, and also follicular ulceration extending throughout the whole extent of the large intestine and into the small intestine where Peyer's patches are affected. This is a very fatal complication of measles, especially if the patient be attacked also by bronchopneumonia, which in some cases appears to be secondary to the enterocolitis. It should, however, be recognized that in some epidemics diarrhœa has been observed during convalescence which is apparently due to elimination of some special toxin and is not particularly lethal; thus Wilischanin[8] observed an epidemic in a girls' school in which ten out of fifty of the patients suffered from diarrhœa during convalescence. It lasted three to five days, and was attributed by him to the elimination of a special toxin. Moreover, a comparatively mild form of enterocolitis is a not uncommon sequela of measles, especially in rickety children, but the disorder is so common in them that its direct connection with the antecedent measles may well be doubted.

The Peritoneum.

Bolognini has recently asserted that in all or nearly all cases of measles there may be observed shortly before the appearance of the eruption a fine peritoneal friction. The pulps of the fingers are placed upon the abdomen, which should be relaxed, and gentle pressure, gradually increased, is exerted, when with a particular degree of pressure on some parts of the abdomen, a slight rubbing sensation will be conveyed to the fingers; if the pressure is increased the sensation disappears. As a rule he found that the phenomenon ceased to be perceptible when the eruption appeared. He considers that it

is due to a condition of the peritoneum analogous to that of the skin in the exanthematous stage, to an enanthem in fact. However this may be, and I have had no opportunity of verifying the observation, there appears to be no doubt that effusion into the peritoneal cavity is an occasional complication or sequela of measles. All the cases on record, so far as I can ascertain, have occurred in girls; in some cases the quantity of fluid has been sufficient to cause marked distention of the abdomen which has persisted for several weeks, but the effusion has eventually been absorbed.

The Kidneys.

Transitory albuminuria may be observed during the febrile stage of measles as of all other acute infectious diseases. In most severe cases ending in death cloudy swelling of the cells of the renal cortex will be found. True nephritis is undoubtedly a rare complication of measles, though Baginsky says that his recent experience leads him to believe that it would be found to be more common than is usually supposed, if it were looked for more carefully. The symptoms—œdema of the lids, face, feet, and scrotum—come on soon after the eruption has faded, and the urine is then found to be diminished in quantity and to contain albumin and casts and in some cases blood. The severity of the nephritis differs very much in various cases, but on the whole the prognosis is good—much better than in scarlatinal nephritis. Loeb found propeptonuria present in nine out of twelve cases at about the time when defervescence was commencing. He found it to be associated in some cases with a condition of dulness and apathy. Anasarca has occasionally been observed without albuminuria.

The Heart.

In severe cases of measles death may be brought about by cardiac failure. The pulse becomes rapid, sometimes irregular; the first sound of the heart is toneless and there may be a systolic murmur. In such cases evidence of myocarditis and of fatty degeneration of the heart muscle is found after death. Pericarditis with effusion, which has in some cases been purulent, has been observed, generally in combination with pleuropneumonia, but such cases are extremely rare. The occurrence of endocarditis producing valvular lesions as a complication of measles is open to doubt, although Dr. Sansom has expressed the opinion that "the influence of measles in predisposing to endocarditis has been much underrated."

J. Hanley Hutchinson[70] has recorded four cases in which organic

mitral murmurs developed during the course of the disease, and Cheadle, in the discussion on Hutchinson's paper, stated that he had found reference to two cases in the post-mortem records of Great Ormond Street Hospital; he had, however, never seen a case during life, and Lee and Sturges questioned whether measles could be recognized as a cause of endocarditis.

Ophthalmia.

The catarrh of the conjunctiva which is so constantly observed during the prodromal and eruptive stages may at that time be very intense, causing great swelling of the lids, from between which a copious mucopurulent discharge exudes. This severe form is most apt to occur in strumous children, and corneal ulceration may ensue, producing corneal opacities, or even perforation and destructive panophthalmitis. At a later stage, as the eruption is fading or during convalescence, phlyctenular ulceration or granular lids may develop and prove very intractable, owing to the deterioration of the general health produced by a severe attack of measles.

Vulvitis.

Inflammation of the vulva and of the orifice of the vagina is a not uncommon complication, especially in delicate or strumous girls of four to ten years of age. Comby[21] met with it twenty-five out of seven hundred and fifteen cases, but attributes this comparative rarity to the fact that antiseptic washes were a routine part of treatment. The inflammation, which is accompanied by a mucopurulent discharge, begins during the acute stage but often persists long after the child has in other respects recovered completely. It is in some cases attended at the outset by ulceration of the labia and much swelling of the parts, which are tender and painful. In such cases micturition is attended by pain and smarting.

Gangrene.

Gangrene of the mucous membranes, skin, or lungs is an occasional complication of measles. Gangrene of the mouth or vulva has become very much less common since the danger of overcrowding and the importance of ventilation have been more generally appreciated by those responsible for the administration of hospitals and asylums for children. The occurrence indeed would at the present day raise a strong presumption that serious sanitary defects existed in an institution in which such cases happened. This opinion is founded upon

the belief that gangrene of the skin or mucous membrane is in most cases due to secondary infection of an inflamed or excoriated surface, an infection which might have been prevented by ordinary care in rendering the surroundings of the patient healthy.

Gangrene of the mouth is described by Rilliet and Barthez as commencing at any time between the third and the thirtieth day. A purplish patch, sometimes covered at first by a blister which is soon ruptured, appears on the internal surface of the cheek. The part affected becomes swollen and brawny, and ulceration commences and extends, always preceded by induration, until the thickness of the cheek is perforated. The gums may be involved and portions of the lower or upper jaw may be exfoliated as a result of the gangrenous process. In the same way the external genitalia in the female may become affected with gangrene involving in an irregular manner the labia and the adjacent skin. Gangrene of the skin, or of the cartilaginous parts of the nose or external ear, was more common in Henoch's experience than gangrene of mucous membranes, but was still even in his large experience very rare. The subjects of gangrene have generally been cachectic children, and this seems to be especially the case when the skin has been the part attacked. The gangrene commences usually some days after the eruption has faded, but may make its appearance earlier. Though, as has been said, usually to be attributed to secondary infection which has found entrance at some superficial lesion, it would seem that it may occasionally be due to thrombosis of arteries or to phlebitis. Of this type an example is afforded by a case recorded by Wunder.[22] The patient was a girl, aged two years, in whom on the tenth day of an attack of measles was found a patch of gangrene the size of the palm of the hand on the right side of the thorax. When the sphacelus was detached it was seen that the periosteum of the ribs was laid bare, as well as a large part of the great pectoral muscle; the gangrenous process had extended also beneath this muscle. Gangrene of the lung is an extremely rare complication. It has been observed only as a secondary consequence of bronchopneumonia.

Septicæmia.

The frequency with which septicæmia occurs as a complication of measles is not well ascertained. It is probable that some if not many of the cases described as "malignant measles" are in reality examples of this mixed infection. This opinion is confirmed by two observations recently published by Folger.[23] Two children, aged respectively eleven months and two and one-half years, died early in the

disease from, as might have been assumed, the severity of the primary infection. In one of the cases (the younger) the only obvious lesion found after death was bronchitis, but the child had died of collapse, not of the ordinary symptoms of bronchitis. In the blood taken from the heart and from the median vein seven hours after death streptococci were found on cultivation. Similar streptococci were found in the capillaries of the lungs, kidneys, and spleen, and in the capillaries, small veins, and (in large masses) in the lymphatics of the tonsils and the subjacent connective tissue. In the other cases pure cultures of a streptococcus were obtained from the blood taken four hours after death from the median vein. In the tonsils were numerous minute abscesses which contained masses of streptococci. In this case there were some centres of bronchopneumonia, but the streptococci were not found in the lungs nor in any other organs examined. Demme and Baginsky[14] have recorded cases of acute osteomyelitis occurring in association with measles, and purpura as well as purpura hæmorrhagica (morbus maculosus Werlhofii) are not uncommon complications. The last-named affection is accompanied in some cases by hemorrhages from the mucous membranes (nose, mouth, etc.), and from the kidneys.

The Nervous System.

The number of cases of nervous disorder which are produced directly by measles is small, and when the enormous number of persons who suffer from the disease every year in civilized countries is remembered, it will be evident that it shows no very marked tendency to attack the nervous system.

Mental Disorders.—Very occasionally the patient remains, after a severe attack in which nervous symptoms have been prominent, in a dull apathetic state which recalls that sometimes seen after typhoid fever, and now and then distinct dementia continues for some weeks or months. Fletcher Beach,[15] in examining the history of 2,000 cases of idiocy, imbecility, or feeble-mindedness found only 37 (1.85 per cent.) which could be attributed to an attack of one of the acute infectious diseases. In no less than 11 of these 37 cases, however, the disease in question was measles. In most of the cases there was a history of insanity, imbecility, epilepsy, excitability, or extreme nervousness in the parents or of a liability to convulsions in other members of the family pointing to a neurotic taint.

Chorea occasionally follows measles; among the 439 cases of chorea analyzed by Stephen Mackenzie for the Collective Investigation Committee of the British Medical Association, measles or measles and

anæmia were the sole antecedent illnesses in 49 (9 per cent. nearly). If a child already suffering from chorea be attacked by measles, the movements usually cease during the febrile attack and sometimes do not recur during convalescence.

Tetany is sometimes observed during the attack of measles in young children and infants, especially in cases in which there have been convulsions at the onset. It may persist for some weeks after convalescence has been established.

Hemiplegia is found after measles as after scarlet fever, but less frequently. Gowers in 80 cases had 7 after scarlet fever and the same number after measles in children under ten years. In 120 cases Osler found 7 after scarlet fever and 4 after measles. This probably more nearly represents the relative proportion of cases attributed to one or other of these causes. When the extreme frequency of measles is taken into consideration it is evident that hemiplegia must be a very uncommon sequela of the disease. So far as the somewhat limited number of cases allows a conclusion to be drawn, the cases appear to be of a milder type than those due to scarlatina. The hemiplegia may come on either during the disease or during convalescence. Of nine cases which have been examined for this purpose, the paralysis is stated to have come on during the disease in four, during convalescence in four, and in one the date of onset is not clearly stated. There does not seem to be any very important difference in the symptoms presented by the two sets of cases, but when hemiplegia comes on during the acute stage of the exanthem it appears to add to the gravity of the prognosis. In all the cases, with one exception, the hemiplegia was first noticed after a fit, or a series of fits. Five of the patients were boys, four were girls. As to the exact date of onset; it was on the second day in two, on the third day in one, and is given as "early" in one; in the cases which occurred during convalescence the date is given with any precision in only one, when it was three weeks after the beginning of the illness.

Muscular atrophy may be a consequence of hemiplegia due to measles in infancy, but the cases do not differ in any way from the ordinary examples of arrest of development produced by hemiplegia from whatever cause if it occur early in life and be of sufficiently grave character. But there is a group of cases, limited in number probably, in which muscular atrophy occurs without hemiplegia, or the general disturbance of the nervous system which ushers in most of the affections produced by the infectious diseases. In speaking of these cases it seems advisable to use the term muscular atrophy, because the pathology does not appear to be very clear. Hughes Bennett[26] suggested the existence of chronic anterior poliomyelitis, but

this theory is not accepted by Erb or Ormerod," and Bennett's case was remarkable in that complete recovery took place. Barlow remarks that of cases of muscular atrophy "in every respect resembling infantile paralysis, we have a fair number of cases on record as sequels of the acute specific diseases." Holmes Coote recorded a case in which after measles there was atrophy of muscles which resulted in talipes equinus, and Buzzard has met with another case after this disease. In Ormerod's cases a father and two of his children were affected in this way after measles, so that predisposition evidently plays a large part in the production of the lesion. The most important clinical point is to recognize that the prognosis is not bad in all cases, but that recovery of function may occur.

"*Pseudo-Ataxy*" *and* "*False Disseminated Sclerosis.*"—Occasionally during the pyrexial stages or during convalescence there is developed, as is the case with most other acute infectious diseases, commonly with great rapidity, a profound affection of the nervous system, characterized usually by loss of consciousness; the patient, if he survive, being found on recovery of consciousness to be bereft of speech and to be suffering from extensive paralysis, paresis, or ataxia. From this condition he may recover completely, or he may develop symptoms resembling those of disseminated sclerosis, but with this difference that the disease is not progressive but rather regressive. In the cases fatal at an early stage, the changes in the central nervous system appear to have been mainly or primarily vascular; and the most reasonable hypothesis to account for those cases in which complete recovery takes place at an early date is that they also are due to vascular derangement. Analogy would suggest that this vascular derangement is produced by the circulation of soluble poisons. Cases also occur occasionally in which the symptoms are those of acute ascending paralysis, which present a very close analogy to well-marked examples of postdiphtherial paralysis. Landouzy has referred to cases of this type, describing them as "extensive, ascending, diffuse, or disseminated." In some of the cases reported it is impossible to meet the objection that the symptoms were really due to concurrent diphtheria, since some of those who have reported cases have not discussed the point or have afforded insufficient evidence. It is, however, unlikely that this explanation would account for all the cases and we have the direct evidence of Barthez and Sanné who state that in eight cases collected by them there could be no suspicion of diphtheria. The symptoms in these cases were palsy of the soft palate, the pharynx, the tongue, and the muscles of the neck. The affection of the muscles was paresis rather than paralysis; in four cases it appeared during the earliest days of the disease, and in

the four others three weeks after. All the cases recovered in from three to twenty days. It is common to assume that diphtherial paralysis, if it do not cause death at an early age, always ends in recovery, that is to say, that the parts paralyzed recover their function. This, however, is not always the case. Some permanent affection of the muscles of deglutition or phonation remains in certain patients. In others there remains some disorder of the motor functions of the lower limbs, spoken of commonly as paraplegia or paraparesis, but in which some degree of ataxia exists. Further, it is important in this connection to note that cases of the type of "false disseminated sclerosis" have been observed after diphtheria (Stadhagen, Schoenfeldt). The analogy, therefore, between the cases of this order which occur in relation with measles and the far more familiar cases of derangement of the nervous system produced by the poisons of diphtheria is therefore very close, and the following classification of such cases which I have advanced elsewhere[28] is useful. Cases of widely diffused nervous affection, lasting for varying periods:

(*a*) Acute disseminated myelitis.

(*b*) Cases presenting at a later date symptoms resembling disseminated sclerosis (false disseminated sclerosis).

(*c*) Cases in which, with some symptoms similar to those of the preceding group, the most prominent symptom is incoordination.

(*d*) Cases of "extensive, ascending, diffuse, or disseminated" paralysis, resembling diphtherial paralysis.

Relation of Measles to Other Diseases.

As has already been stated, measles is a disease which undoubtedly conduces to the development of tuberculosis, or, in the words of Comby, "*La rougeole est une maladie essentiellement tuberculisante.*" In bringing about tuberculosis, pulmonary or general, it acts in two ways. By the damage inflicted on the mucous membranes and on the lungs and by the general lowering of health it diminishes resistance, local and general, to tuberculous infection. Or, if the individual be already suffering from chronic glandular tuberculosis, it favors the generalization of the infection. Some evidence of the frequency with which children in apparent health are the subjects of latent tuberculosis is afforded by the statistics of Geill[29] from the Blegdams Hospital in Copenhagen. He made the post-mortem examination of 584 children under fifteen years, who died during a period of three years from various acute infectious diseases, and found naked-eye evidence of tuberculosis in 198, or 34 per cent.; under two years of age the per-

centage was 21.2; over that age, between 46 and 47 per cent. The lymphatic glands were affected in all the 198 cases, and were alone affected in 79.

It has been maintained that a disease undistinguishable from whooping-cough is frequently a sequel of measles. Some of the cases upon which this opinion is founded are probably examples of paroxysmal cough due to pressure exerted by enlarged mediastinal glands. The resemblance of the symptoms is indeed so close that Guéneau de Mussy argued that the true pathology of whooping-cough was a specific enlargement of the tracheobronchial glands. With regard to true whooping-cough, the truth appears to be that measles predisposes to whooping-cough and *vice versa.*

Measles may be preceded or followed by scarlet fever at a short interval, but it is probable that some of the cases, supposed to be examples of this occurrence, are in fact due to an error of diagnosis (*see* Diagnosis). The concurrence of scarlet fever with measles very much aggravates the prognosis; thus Hase in ten such cases observed very high fever with severe complications, and lost eight of the patients. The eruption of varicella has also occurred during the progress of a case of measles, but the concurrence does not appear materially to modify the prognosis.

Measles and Pregnancy.

It has been asserted by some that a pregnant woman is not liable to contract measles, but this statement rests upon a misapprehension. The occurrence is rare, owing in all probability to the fact that most women in civilized countries have suffered from the disease in childhood and have thus acquired immunity. The disease develops in a pregnant woman after the usual period of incubation, and the symptoms do not differ in any respect from those observed under other circumstances. The most common and serious complication is bronchopneumonia. In many cases on record, abortion or labor has occurred either at the onset of the disease or more commonly during the eruptive stage, whatever the stage of gestation which may have been reached. The patient is seized with labor pains at about the time the rash comes out. Intrauterine infection appears to be the rule, so that the child may be born with the eruption upon it, or, if the mother is in the prodromal stage when birth takes place, the child will probably have the eruption at about the same time as the mother, or a day or two later. Only in very rare cases has the eruption appeared at such an interval as to render it probable that the child contracted the disease from the mother after birth. Puerperal septicæmia has been observed after delivery, but much less

often than in puerperal women attacked by scarlet fever. Severe hemorrhage after delivery is a possible complication which must be borne in mind. Measles may develop during the lying-in period after delivery. In the rare instances in which this has been observed, it has caused much anxiety, since the diagnosis from septicæmia accompanied by rash has been at first difficult.

The prognosis of measles in pregnant women is favorable, the only reservations being that (1) if miscarriage does not occur, bronchopneumonia, should it develop as a complication, is liable to cause greater embarrassment of the respiratory function, owing to the distention of the abdomen, and that (2) if miscarriage does occur, the patient is rendered rather more liable to contract septicæmia, since the systemic infection of measles appears to predispose to septic infection. A pregnant woman, especially one advanced in pregnancy, who has not acquired immunity by an attack in childhood, should therefore be advised to avoid contact with children suffering from measles.

Diagnosis.

The diagnosis of measles, which it may be exceedingly important to make in the prodromal stage, since the infection is then very active, is often difficult at that period. In a mild case the symptoms resemble those of coryza very closely, but in an average case of measles the child is from the first more depressed than with ordinary coryza and the temperature is higher. But the practitioner must not let himself be deceived into supposing that the remission in the temperature and general symptoms which occurs usually on the second or third day of the invasion of measles, marks the disappearance of coryza. *Influenza*, if accompanied by much coryza, may resemble very closely the onset of measles, and the resemblance may be the closer if there be much depression and high temperature. The most characteristic single symptom of the prodromal stage of measles is photophobia. In a child who has not previously suffered from measles the sudden onset of coryza accompanied by dread of light would raise a very strong presumption of measles, and it would be imprudent to hazard a suggestion of influenza even if that disease were prevalent. In schools in particular it is desirable to isolate on suspicion. When one case has occurred, a careful watch must be kept on all susceptible children who have been in contact with the patient, and any attack of the nature of coryza, however mild, should be held to be under suspicion of marking the invasion of measles. When the erythema of the palate (enanthem) appears early, it will be of assistance in confirming a diagnosis of measles.

The bright erythematous flush which sometimes precedes the true eruption of measles may give rise to a suspicion of *scarlet fever;* but the rash is usually limited to the face and less brilliant, the skin is less pungently hot, and the affection of the throat is milder. Moreover, the child will usually have already been ill for several days, which would render scarlet fever unlikely. However, in any case in which a doubt is felt, the only prudent course is to isolate the patient as though the diagnosis of scarlet fever were assured, until the doubts are set at rest by the course of the illness. The difficulty during the eruptive stage is as a rule very much less, since the eruption, taken together with the general symptoms, can leave little doubt as to the nature of the malady. The chief source of error is the resemblance between a mild attack of measles and a case of *rubella* in which the eruption is of the morbilliform type, as is usual. In rubella there are either no prodromes or they are of an exceedingly mild kind, and even at the onset of the eruption the patient does not as a rule feel very ill nor is the temperature much raised.* Coryza is less and photophobia generally absent. The rash comes out more rapidly and not by a gradual spread from above downwards as in measles, there is no enanthem, and the enlargement of the lymphatic glands is often considerable (greater than in measles) and quite out of proportion to the pharyngitis, if this be present. There is as a rule little or no bronchitis, and the tongue is clean or only very slightly furred. *Roseola* and *erythema*, whether idiopathic or symptomatic, may give rise to some hesitation. The onset of idiopathic roseola may be preceded by some slight elevation of temperature (100° to 102° F.), restlessness, rapid pulse, furred tongue, and in some cases redness of the palate. The eruption appears early, usually in a few hours, and is very irregular in form and distribution. It may resemble the true exanthem very closely, but the general symptoms are less severe, the temperature falls soon after the rash appears, there is no photophobia, and coryza is not a part of the attack. The prodromal rash of *variola* may present a certain resemblance to the eruption of measles, and Osler admits that it cannot always be distinguished from it. The mistakes on record, however, are instances in which the exanthem of measles has been supposed to be the prodromal rash of smallpox. Somewhat similar rashes may occur during the period of invasion of varicella and vac-

* An experienced country practitioner once remarked to me that he had often been much assisted in coming to a diagnosis by observing that when first called to a house in which children were suffering from scarlet fever he found them in bed, if they were suffering from the early stage of measles they were sitting listlessly in a chair or lying on a sofa in their nursery, but that if they had German measles they met him in the hall and showed him their spots!

cina, of the algid stage of cholera, while *roseola febrilis* is a recognized complication of diphtheria and malaria.

The rashes which may follow the injection of diphtherial antitoxic serum and antistreptococcal serum have sometimes given rise to doubt. Of rashes due to drugs, that produced by chloral most resembles the exanthem of measles, but the resemblance is not very close and this is still more true of the antipyrin rash occasionally seen in children. *Acute general eczema*, which occasionally spreads in an epidemic fashion, may present a certain resemblance to measles on superficial examination, especially if it be complicated by ophthalmia, as is sometimes the case. A careful examination of the character and distribution of the eruption, which is usually accompanied by some scabbing or crusting even in an early stage, will, in conjunction with the general considerations mentioned above, render any error impossible.

In all such cases all the circumstances of the case, the risks of infection, and so on, must be taken into consideration. As Crocker has well said: "It must always be borne in mind that the diagnosis of all the exanthemata should never be made on the rash alone, and indeed not on any one or two symptoms, as there is great variation in the development of every feature of these diseases, as regards incubation, prodromata, and general symptomatology, and in doubtful cases a conclusion can only be arrived at by carefully weighing the symptoms as a whole, and noticing accurately how the supposed exanthem differs from the usual type, remembering that the more fully the rash is developed the less likely are the other criteria to fail in a real exanthematous fever."

Prophylaxis.

In considering the prophylaxis of measles we must look at the question from two points of view. We have to consider the prevention of the spread of the disease, an undertaking which is at the present moment the despair of the medical officers of sanitary authorities, and the prevention of the large mortality which the disease produces. The latter object may be sought with more hope of success, for the mortality produced by measles is mainly due to its complications, of which most may be prevented, or at least very much diminished in severity.

The great difficulties in the way of applying the methods of isolation and disinfection, ordinarily found effectual for checking infectious diseases, to the prevention of the spread of measles are the extremely infectious character of the disease, especially in the early stage when the symptoms are not, in the absence of an epidemic, sufficiently dis-

tinctive to allow a positive diagnosis to be made, and the extraordinary rapidity with which an epidemic of measles assumes large proportions. To these may be added the indifference of the public and the small estimation in which measles is held as a rule by them.

Upon the valuable report "On the Control of Measles" by Dr. Theodore Thomson,[1] to which reference has already been made, and upon a criticism of its conclusions and recommendations contained in a paper read by Dr. Kenwood[2] before the Sanitary Institute, I shall mainly rely in what follows. It should be said that Dr. Theodore Thomson's report was written after a prolonged and careful inquiry, during which he visited a number of localities where various schemes of prevention had been tried, and after a complete examination of the documents and of the results attained. It will be well to give first of all the means recommended by Dr. Thomson for obtaining control of measles, and it will be convenient to do this in the following tabular form, for which I am partly indebted to Dr. Kenwood's paper. The series of propositions advanced by Dr. Thomson may be thus summarized:

A. Sources whence information may be obtained as regards occurrence of measles:

1. The adoption of compulsory notification by the medical attendant and householder. This must be regarded as defective for reasons given below, but the information thus received may be used as a clew to the detection of other cases. Efforts must be made to insure systematic notification by the householders; as by the distribution through the medium of schools, or by placarding, of handbills impressing on householders their duty, and their liability if they fail to notify.

2. Careful inquiry in every instance to trace, where possible, the source of infection; supplemented by house-to-house visitation in the immediate neighborhood, where necessary.

3. Notification by school authorities of any known or suspected cases of measles, of which they have information, and also of the names and addresses of absentees from school. This should be made obligatory in municipal schools, and efforts should be made to enlist the coöperation of the masters or mistresses of private schools and the teachers in Sunday-schools. The information needs to be given systematically, that is to say, during interepidemic periods, as well as when epidemics of measles prevail. Sanitary authorities in receipt of information derived from school authorities should, it need hardly be said, regard knowledge of cases in this way reported to them as possible clews to the detection of other and unknown cases.

4. Information, general or particular, from persons and organizations rendering assistance medical or eleemosynary to the poor, from the clergy, and from church organizations generally.

B. Measures whereby extension of measles within the invaded dwelling may be limited.

1. Every household known by the sanitary authority to be invaded should at once be visited by an officer of the Health Department for the purpose of ascertaining what steps have been taken towards attainment of proper isolation of the sick person, and of advising, if necessary, further efforts in the direction of safeguarding other inmates of the dwelling. In addition to verbal instruction on this subject, printed forms containing similar advice may with advantage be left with the householder. During the infectious period the patient, if not removed to a hospital for infectious diseases, should be kept apart from other members of the family, in a suitable room and in charge of an attendant who should have no personal communication with other inmates of the house; and precautions of cleanliness and disinfection should be taken.

2. Frequent visits should be made to the household by officers of the sanitary authority, with the view of seeing that precautions against spread of infection are not relaxed so long as there is danger of the disease being communicated to others. Such visits should serve also to aid in the early detection of other cases in the same family. For not less than fourteen days after disinfection of the invaded dwelling members of the household should be kept under observation, and they should receive instruction to communicate at once with the medical officer of health on the appearance among them of any suspicious symptoms.

3. Where it is found impossible owing to inadequate house accommodation or other reasons to isolate the sick properly, it is most desirable that the patient, if the state of his health permit, should be at once removed to a suitable hospital.

4. After recovery of the patient or after his removal to a hospital, the room or rooms that have been occupied by him, and all articles that may have been infected, should be thoroughly disinfected.

C. Measures whereby extension of measles throughout the invaded district may be checked.

1. The notification by the Health Department of the occurrence of measles to school authorities.

2. The exclusion from school for a prescribed period, or pending the production of a medical certificate of (*a*) all members of invaded households; (*b*) children known to have been in personal communication with houses in which measles is known to have broken out;

(*c*) children of households not yet invaded but in close relation with houses already invaded.

3. Closure of elementary schools. To be effectual this must include all private schools for young children and all Sunday-schools. If it cannot be made universal it is not worth attempting. To close the day-schools and leave the Sunday-schools open may be expected to have the effect of spreading the epidemic over a longer period of time without producing any such diminution in the total number of cases as would compensate the community for the great inconvenience caused by the closure of the elementary schools. School closure, if resorted to, should not be adopted while there is reasonable prospect of effectively controlling measles by other means; nor on the other hand should it be postponed until prospect of benefit from this measure has wellnigh disappeared.

4. Precautions with reference to library books. The librarians of public libraries should be systematically informed by the sanitary authority of the names and addresses of all persons known to be suffering from measles, with a view to not supplying books to any member of an invaded household until further informed by the sanitary authority that this may be done with safety.

5. Prohibition of those residing in invaded households from carrying on their occupations, when such a step appears necessary.

6. Instruction of the public upon the gravity of measles, especially among infants and young children.

7. Temporary addition to the sanitary staff during times of epidemic prevalence of measles, for the purpose of effecting the necessary inquiries, visits, disinfections, etc.

It will be seen that the measures suggested are of a most elaborate character, involving, as they do, the ready coöperation of the governing authorities, masters and mistresses of all schools, of the clergy of all denominations, of the public libraries and of the individual householders with the municipal Health Department or other sanitary authority of the town or district. Yet Sir Richard Thorne, the principal medical officer of the Local Government Board, in his official minute commending Dr. Theodore Thomson's report, writes: "It cannot be too clearly understood that good result is not to be expected from the adoption of any single one of these several measures; and that if any approach to complete success be aimed at, each one of the several measures indicated must be regarded as necessary and supplementary to the others."

With regard to the practical value from the public-health point of view of the enforcement of the notification to the sanitary authority of the district of every case of measles, much difference of opinion

exists. Dr. Kenwood made a special inquiry in 1897 and he found that in England 77 districts had adopted compulsory notification before March, 1892, and that by March, 1897, the notification had been revoked in 32, or 41.5 per cent. Of the remaining 45 districts only 2 could, after a trial of five years, produce any satisfactory statistical evidence of its value. In 12 it was believed that the measure had had some value, while in the remaining 13 the medical officers were unable to say that the measure had been of value.

The failure of notification is due to many causes. One is the ease with which an epidemic may be started by patients who have not yet reached a stage in which they present any recognizable symptoms, or indeed any symptoms whatever. A very striking example of this is given by Dr. Fenton, the medical officer of health for Coventry, England.

"After a period of comparative freedom an outbreak was started as follows: Thirteen children attended a dancing class one afternoon, including three of my own and two of a friend's who had just arrived in the district, and who had been exposed to the infection of measles before arriving. These two children came to my house and spent the evening in my presence. There was nothing to attract my attention to their condition, and indeed, so well were they that they had walked six miles in the morning, had danced in the afternoon, and walked home about one mile at night. Next day they both sickened and developed measles. Of the remaining eleven children two were presumably immune, having previously suffered from measles, but the whole of the nine developed measles during the following fourteen days. In my report on this subject are the following remarks: 'It would thus appear that infection may be contracted from an individual who, though having the disease in the system, has not yet shown the slightest indication of it; bearing in mind this, and also that the above-mentioned outbreak occurred among the more observant and intelligent classes, it cannot be surprising if poorer and less careful parents send their children to school occasionally after the infectious stage has set in, and that the presence of such children in school or in public places should rapidly light up an epidemic quite beyond the control of the sanitary authority.'"

Notification can be of value only if effective use can be made of the information thus obtained. Its logical consequence should be isolation of the sick. Isolation in infectious hospitals is almost if not quite impracticable, because the number of beds which would have to be provided would be very large in proportion to the population. When an epidemic is once on foot the number of cases runs up by leaps and bounds, so that whereas in one month they may be num-

bered by tens, in the next they may be numbered by hundreds. Thus in Edinburgh the difference between one month and the next has been eight hundred, and both in this city and in Birkenhead, from one-third to one-half of the notifications made in a year have been received in a single month. Not only would it be necessary to maintain a large hospital all the year round, but the staff must also be large. To quote the words of Dr. Kenwood: "Think of the enormous difficulties and expense of administration of a hospital, say of two hundred and fifty beds, with a baby under five in seventy-five per cent. of them, and a baby of two in a considerable number! A large hospital, with an exceptionally large staff, would have to be prepared, almost at any moment, to receive measles patients in every community of twenty thousand; and this hospital, and at least a large part of the staff, would figure as a heavy permanent expense to the community, although for many months at a time it might not be required."

Among the well-to-do classes a great deal may be done to obtain effective domestic isolation. The patient should be nursed in a separate room by a competent person who should not be allowed to come into personal communication with other inmates. But among the poorer classes who live in tenement houses or small cottages this is not, as a rule, practicable, and more may be done to check epidemic outbursts of measles by getting control of the elementary schools, especially those for infants and the Sunday-schools, than by any other one means. The Health Department ought to be able to hear at once of every absentee, and should make immediate inquiries to ascertain whether the cause is illness. In this way it would get to know not only of the earliest cases of measles, but also of whooping-cough, scarlet fever, diphtheria, and "sore throat." If the case be one of measles, there should be power to exclude all children in the house from school, as recommended by Dr. Theodore Thomson, and at the same time information should be conveyed to neighbors by handbills and through the press as to the gravity of measles in infants and young children, the precautions which should be taken, and the need for early medical treatment. Schools are the great centres of dissemination of measles, as of some other infectious diseases, and the regular medical inspection of children in elementary schools might be trusted to do much towards checking epidemics at their commencement. When an epidemic has begun, daily medical inspection is the only substitute which can be suggested for closure of the schools, should that not be found expedient. One of the advantages which may justly be claimed for a system of notification is that it would make the Health Department aware of the occurrence of cases in houses from which food was retailed (milkmen, confectioners, etc.),

and would enable it to take special precautions. In small country communities also where the growth of an epidemic of measles is less rapid, the system is capable of rendering considerable service if extended over a sufficiently wide area. Notification also enables the Health Department to provide for the effective disinfection of houses after the patients in them have recovered or have been removed.

Other precautions which may be taken by the Health Department are sufficiently indicated in the scheme quoted from Dr. Theodore Thomson's report. The following handbill, issued by Dr. J. B. Russell for the Glasgow Health Committee, which is printed with the omission of three concluding paragraphs not of general application, may be found useful as a model:

HINTS ABOUT
THE
PREVENTION OF MEASLES.

The Committee on Health of Glasgow hope that parents and others will read this paper carefully, and adopt the instructions which it contains, and any others given by the medical attendant having the same end in view.

Measles is a dangerous disease, one of the most dangerous with which a child under five years of age can be attacked. It is especially apt to be fatal to teething children. It tends to kill by producing inflammations of the lungs. It prepares the way for consumption. It tends to maim by producing inflammations of the ears and eyes.

In Glasgow, during the last five years, measles has caused three deaths for every one which has been caused by scarlet fever. Only one infectious disease has been more destructive of life, viz., whooping-cough. Measles has carried off more than four times as many persons as enteric fever.

It is therefore **a great mistake to look upon measles as a trifling disease.**

The older a child is the less likely is it to catch Measles; and, if it does, the less likely is it to die.

If every child could be protected from measles until it had passed its fifth year, the mortality from measles would be enormously decreased.

It is therefore **a great mistake**—because, as a rule, children sooner or later have measles—**to say "The sooner the better,"** and to take no means to protect them, or even deliberately to expose them to infection.

It is wrong for mothers with children in arms to go into houses where measles exists.

Every child ill of measles ought at once to be put to bed and kept warm. The

mildest cases may be made serious by a chill. Measles is, for this reason, most dangerous in winter and spring.

A case of measles continues infectious for at least three weeks after the appearance of the rash. During that time separation from the healthy ought to be secured either by removal of the sick to hospital or by isolation at home.

Isolation means not merely a separate room for the sick, but the withdrawal of apparently healthy children of the same family from school (day and Sunday), and the exclusion of strange children from the house.

The isolation, as far as possible, from other children of all children belonging to the same family is more necessary in the case of measles than of any other infectious disease, because of this peculiarity—**for days before the rash comes out, the child is highly infectious.**

School teachers especially ought to be familiar with the appearance of children in this stage of measles.

The eyes are watery, glistening, and sensitive to light; there is a ringing cough, sneezing, and running from the nose, with a flushed face; in short, all the signs of a bad "cold in the head."

No child showing these symptoms ought to be allowed to go to school.

Any child observed at school with these symptoms ought to be sent home at once. Such children are to be looked for more particularly in the Infant Department. J B. R.

SANITARY OFFICE,
MONTROSE STREET, GLASGOW,
January, 1897.

The model by-laws approved by the French Government for dealing with the prevention of epidemics in connection with primary schools prescribe" that every child attacked by fever should be sent away from the school, or if an in-pupil to the infirmary, and upon the advice of the doctor charged with the inspection, the brothers and sisters of the child, and even all children of the same house should be kept away from the school. The family of the child must receive a notice as to precautions to be taken against possible infection of other children, and as to the necessity of not sending the child back until it has bathed or washed with soap several times and until its clothes have undergone either disinfection or complete washing in boiling water.

Children who have been ill must not return to school without a medical certificate and not until after a period of time has elapsed since the beginning of the fever equal to that prescribed by the instructions of the Academy of Medicine of Paris.

The special regulations prescribed as to measles are that all children attacked must be forbidden to return to school for sixteen days, and their books and copy-books, toys, and other objects which may

have been contaminated in the schools must be destroyed by burning. The class-rooms must be disinfected and when several cases occur within a few days, in spite of all precautions, either the schools must be closed, or exclusion of children under a certain age becomes necessary. When "licenciement" is considered necessary, a notice containing instructions as to the epidemic disease which has necessitated the exclusion is to be sent to each family. With regard to the disinfection of class-rooms, the instructions are: Wash the class-room walls and floor with an antiseptic. Disinfect by atomization all maps, etc., hung on walls. Disinfect by washing tables, seats, and furniture generally, completely disinfecting the desks of patients, destroying books, toys, etc., by fire.

The *prevention of complications* is in the vast majority of cases of measles the most important part of treatment also. The two main points are to attend to the cleanliness and ventilation of the room and to the "toilette" of the mouth, throat, nose, and eyes, but it is undoubtedly advisable to keep the child in bed from the onset of the symptoms until desquamation is over, or if this is not noticeable, for about ten days altogether. The danger of exposure to cold may easily be exaggerated and Vierordt[7] recommends that the child should be taken out of doors in its bed on warm, sunny, still days, of course carefully protecting the eyes from light. Care should be taken to avoid great variations in the temperature of the room or exposure to direct draughts. In cold weather the temperature of the room should be maintained at about 65° F., and the air should be kept moist. This may be effected by placing a pan of water on a small stove or spirit lamp, by the old-fashioned plan of keeping a kettle boiling slowly on the hob, or by the use of a steam spray. The last-named plan has the advantage that some aromatic disinfectant may be added to the water; this will at least have the effect of correcting the unpleasant odor which pervades a room in which a case of measles is being nursed. When possible it is a good plan to use two adjoining rooms, the one by day and the other by night; the room not in use being cleaned, dusted with a damp cloth, and thoroughly ventilated. The entrance of dust and smoke should be guarded against, as both tend to increase the irritation of the mucous membranes. Dryness of the air not only contributes to the greater irritation of the mucous membranes, but also favors the dissemination of dust and perhaps also of the microbes to which bronchopneumonia, the most frequent and dangerous of complications, is due. The person nursing the child should wear a cotton dress and should pay the greatest attention to personal cleanliness. As the bronchopneumonia is undoubtedly communicable, it is undesirable that a child suffering from this

complication should be nursed in the same room as other patients suffering from measles, or that the same drinking utensils should be used. Since it has been shown that the microbes associated with bronchopneumonia are present in the mouth in more than half the cases of measles, the use of antiseptic mouth washes has become very general as a routine measure. The use of a solution of boric acid or borax (one to two per cent.) three or four times a day as a mouth wash is a simple precaution and rather grateful to a patient old enough to resort to it. In some epidemics there seems to be a special liability to ulcerative stomatitis and to diphtheria, and when this is the case, the use of a mouth wash should be made a rule, and in infants the mouth should be washed out with a syringe or by spray. It is particularly important to carry out these precautions in those children in whom respiratory complications of a severe type are liable to occur either on account of their age (six months to six years) or because they are subjects of rickets or tuberculosis.

The following account of the precautions in use against measles and its complications as well as against other infectious diseases at the Hospice des Enfants Assistés, Paris, illustrates some of the modes in which a hospital or any other large building with large rooms may be utilized as a place for treating measles, and shows how much can be done even under very unfavorable circumstances to prevent complications, especially diphtheria and bronchopneumonia—and thus to diminish the death-rate of the disease. The case-mortality from measles was in this hospital in past years very high; during the years 1869–72 it reached 48.72 per cent.; in 1878, 42.64 per cent., and during the years 1882–85, 44 per cent. In children's hospitals in Paris the mortality averaged only 26.6 per cent., thus proving that the high death-rate in the Hospice could not be due to the severity of the epidemic type. Statistics showed that diphtheria and bronchopneumonia were to a great degree responsible for this high death-rate, for during the six years ending 1891, of the total number of cases of measles 14.39 per cent. died from diphtheria, 23.75 per cent. from bronchopneumonia. Special precautions were consequently taken against these two complications, and these, combined with general sanitary improvements in the treatment of patients suffering from measles, resulted in a reduction of the death-rate from over 40 per cent. to about 20 per cent.

1. *General Precautions.*—The children were made clean and were kept very warm by swathings of thick cotton under the nightgown. All the attendants, of whom there was about one to every four children, and residents were required to wear clean Holland overalls; the visiting physician wore a long white apron, over this a long Holland

coat and an extra Holland coat which he changed in each ward. The use of antiseptics was general and very thorough. All children newly admitted into the Hospice were thoroughly cleansed before being sent into the schools. All heads the least suspicious were done up in gauze bandages; and all children suffering from impetigo or rashes of the slightest description were treated in a like manner. All cases of discharge from eyes, nose, or ears, were bandaged or plugged with wool.

2. *Special Precautions.*—All cases of bronchopneumonia were isolated in "boxes." These were spaces partitioned off by glazing, about eight feet in height and open at the top to the ward (Fig. 8).

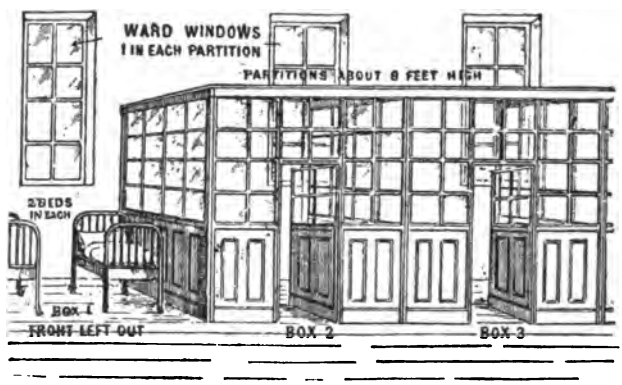

FIG. 8.—Isolation Boxes for Cases of Measles with Bronchopneumonia.

Each contained a door and a window of the ward. There were two beds in each, with their heads about two feet from the wall. These were not kept entirely for cases of bronchopneumonia but were mainly used for them because, (1) that disease was considered very infectious; and (2) isolation was thought to diminish the severity of the attack. There was also a systematic application of antiseptic precautions to the mouths of the patients and to the drinking-vessels used by them.

The death-rate from diphtheria had been enormous up to May, 1892. At that date special precautions were enforced and the deaths diminished from twenty-seven during the first four months of the year to one during the last eight months, and in the year 1893 not a single case arose in the Hospice. These precautions embraced effective disinfection of linen, boiling of toys, frequent disinfection, and cleansing of each ward, and personal disinfection of nurses and others on duty in the diphtheria wards. A special isolation block had been

built in 1886, but this alone did not bring about any diminution in the death-rate until the special antiseptic precautions were instituted.

In the Hôpital des Enfants Malades, Paris, another precaution was instituted in infectious cases. At meal-times a mackintosh sheet was spread on the bed and an oblong galvanized wire basket with a tall handle (Fig. 9) was placed on it. This basket contained a basin for the patient's food and had small divisions at the sides for the salt, glass, etc. It was carried straight to the kitchen after meals and plunged into boiling water.

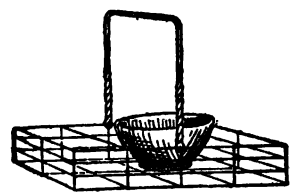

FIG. 9.—Wire Basket for Carrying Meals to Patients with Infectious Disease, in Use at the Hôpital des Enfants Malades in Paris.

Treatment.

In mild cases of measles of the ordinary type the treatment should be of the simplest kind and should consist chiefly in mitigating the discomfort which the patient suffers, owing mainly to the thirst, cough, and photophobia, and in the observance of the prophylactic measures already mentioned. Thirst is in many cases very distressing and the patient should be allowed to drink as much as he likes of weak lemon water, water acidulated with fruit syrups, such as raspberry vinegar, or of a beverage made by adding one or two per cent. of phosphoric acid and perhaps a little syrup to water. If the child can be induced to take a considerable quantity of fluid, this will have the further good effect of increasing the quantity of urine. The diet should be simple, the simpler the more severe the disease and the greater the fever and loss of appetite. The liability to the production of diarrhœa, especially in epidemics in which this is frequent, or in hot weather, or when the individual is predisposed to intestinal catarrh, must be borne in mind. Milk is the best staple diet, but should be given diluted with water, soda water, or slightly aërated mineral water. Alcoholic stimulants are not as a rule required and unless given in doses large enough to produce the hypnotic effects of alcohol rather tend to increase the irritability and sense of discomfort. Antipyretic drugs must also be used with discrimination. In a robust child with high fever a few full doses of antipyrin will cause a fall of from one to three degrees, with a considerable amelioration of the general symptoms, but in weakly children, or when bronchopneumonia has declared itself, these full doses are not free from danger, and if it be thought necessary to give an antipyretic drug, quinine is to be preferred. Antiseptic sprays and mouth washes are not only of service as prophylactics but soothe the irritation of the

fauces and so tend to diminish cough. For this purpose a linctus containing ipecacuanha and a small (sedative) dose of antipyrin, or a few grains of potassium or sodium bromide, or a minute dose of codeine may be given at short intervals. A warm bath should be given at the outset of the symptoms, and throughout the attack great attention should be paid to personal cleanliness.

Laryngitis, if mild, should be treated with sprays, or by the steam tent. When more severe, or complicated by attacks of croup, relief may usually be obtained by the application of a very hot fomentation to the front of the neck. This should make the skin, for the time, brilliantly red. If after one thorough application it becomes necessary to repeat the fomentation, it must be used at a rather lower temperature. In robust, full-blooded children in whom there is congestion of the face and neck, much relief will generally be obtained by the application of one or two leeches immediately above the sternum. Membranous laryngitis may call for intubation or tracheotomy.

Stomatitis and pharyngitis must be treated by antiseptic sprays or mouth washes, repeated at frequent intervals, and by the application of glycerin, of borax, or of a mouth salve consisting of equal parts of lanolin and olive oil, containing boric acid, thymol, or eucalyptus.

For the so-called *capillary* or *suffocative bronchitis*, the treatment which gives most immediate results is dry-cupping, which should be followed by hot fomentations or poultices. Stimulant expectorants should be avoided, and care should be taken to keep the extremities warm. Unless diarrhœa is present, a laxative should be given, and for this purpose castor oil is to be preferred. In serious cases general stimulants frequently become necessary and hypodermic injections of camphor, strychnine, or caffeine are to be preferred to alcohol, which has too marked a hypnotic influence. The treatment of bronchopneumonia complicating measles does not call for special discussion, inasmuch as it is identical with that same condition produced by any other cause.

The room in which the child is nursed should be darkened sufficiently to relieve the discomfort due to photophobia, but not so much as to interfere with the proper nursing and inspection of the case. Too dark a room also has a depressing effect upon the patient. The condition of the conjunctiva should be watched carefully and any excessive conjunctivitis treated by antiseptics and astringents and the eyelids anointed with a weak ointment of yellow oxide of mercury (one per cent.). Phlyctenular ophthalmia must be treated by methods ordinarily employed. Vomiting and diarrhœa in the early stage are best treated by a small dose of calomel or castor oil, followed by

a few doses of rhubarb and soda with a stomachic such as peppermint or ginger. The profuse mucous diarrhœa of a later stage is often very intractable. When colic is severe a small dose of castor oil, followed by minute doses in emulsion guarded by opium, should be given and hot applications made to the abdomen. If the condition become subacute or chronic, the castor-oil emulsion may be continued with the addition of ipecacuanha, or small doses of magnesium sulphate prescribed, with an aromatic. Astringent injections or suppositories may also be required. The abdomen should be enveloped in a flannel binder, and care should be taken to keep the lower limbs and feet warm. The diet should be simple, but milk is not always well borne. In such cases, underdone meat scraped to a fine pulp, and thick gruels should form the main part of the diet. It will often be found that recovery can be insured only by adding to the diet a considerable quantity of fresh fruit, which must, of course, be thoroughly sound.

In the severer forms of the disease in which symptoms of nervous irritation, restlessness, sleeplessness, or delirium are prominent, the patient should be kept cool, the bedclothes should be light, and sleep may often be induced by applying a cool compress to the front of the chest, or by a cool or hot pack to the lower limbs. In the rare cases in which the *cerebral symptoms* are pronounced, and especially in those in which there is loss of consciousness with constant delirium, flushed face, and rapid tense pulse, more energetic hydropathic treatment is called for. In the first place a bath at 90° F. (32.2° C.) should be given and repeated at intervals of six to eight hours. If there be much nervous depression which is not relieved by the simple bath, or if there be signs of heart failure, a douche of cool water should be given to the nape of the neck just before removing the child from the bath. If with a comparatively low temperature the symptoms of nervous depression are severe, the application of a mustard bath may be tried, or of a hot bath followed immediately by a cold affusion to the head and neck.

Convulsions at the onset of the illness need not cause apprehension unless they are severe, but if continued they are of very bad augury. Bath treatment is not to be recommended in such cases, but the ice-bag to the head is often useful. A condition of apathy and drowsiness with occasional convulsions and congestion of the face may often be treated with advantage, even in quite young children, by the application of leeches to the mastoid, and this treatment may be adopted without hesitation in older children and in adults, especially if the patient be of a robust type. Of internal remedies for cases marked by cerebral excitement, none is superior to antipyrin. If the general

condition of the patient warrants the use of this drug, it is best given in a single full dose, appropriate to the age, in the afternoon. When with a temperature which is high there are symptoms of adynamia, or the patient is feeble, antipyrin must be replaced by quinine, which, though less effective, is less depressing. Of the sulphate the dose should be one to two grains three times a day for each year of age. If diarrhœa be present, the tannate is preferable, but the dose must be from twice to three times as large as that of the sulphate.

Attention should be given to the condition of the *skin* throughout the attack, and excoriations about the mouth, or impetigo which is very apt to occur as the eruption fades, should be treated by antiseptic ointments, among which none probably is superior to a weak white precipitate ointment (one per cent.). Itching of the skin, which sometimes leads to impetigo owing to the scratching which it provokes, may be relieved by rubbing with oil containing a little eucalyptus or with carbolic vaseline. During desquamation the child should be given warm baths, after each of which it should be put to bed for a short time.

Slight *epistaxis* in the early stage does not call for treatment. If it continue, it may usually be arrested by injection of hot water, as recommended by Trousseau. In some cases it comes from the anterior part of the nasal cavities and may be arrested by plugging the nostrils with corrosive sublimate absorbent wool, smeared with an antiseptic ointment. In very rare cases it may be necessary to resort to the injection of solutions of zinc sulphate or iron perchloride. Plugging the posterior nares ought not to be resorted to except in cases intractable to other means, as the plug quickly becomes horribly foul and is liable to set up septic pharyngitis and otitis.

Other local complications of measles must be treated upon ordinary principles laid down in other parts of this Work, always remembering that vigorous antiseptic treatment will in ninety-nine cases out of one hundred arrest the process if instituted early enough.

Much may be done to prevent the development of *otitis* and to obviate its more serious consequences. The liability to this complication is one of the grounds upon which the routine use of antiseptic mouth washes and gargles is recommended. A patient old enough to do so should be encouraged to "blow his nose" frequently, as by this means the accumulation of secretion is prevented and the forcible passage of the air through the nasopharynx towards the nose helps to loosen discharges accumulating on its walls. If the child is too young to do this, or if the nasopharynx is blocked by adenoid vegetations and enlargement of the faucial tonsils, Downie recommends the use of Politzer's inflation bag. The child being in the recumbent

or sitting position, he is directed to open his mouth and to breathe out strongly, or to say "Ho" or "Hic," and at the same moment the air is forced along the nose. A large quantity of secretion may thus be dislodged and thrown into the mouth. He advises that this should be done in all cases of blocking of the nasopharynx, and that the onset of dulness of hearing or of pain or noises in the ear should in every case at once lead to its employment. The danger of rupture of the membrane may, he thinks, be disregarded. It rarely happens, and if it does the resulting slit-like perforation heals rapidly. Whereas, if the rupture into the tympanum is produced by the suppurative process, it is generally circular and the damage to the drum membrane is irreparable. It must be confessed, however, that in quite young children these manipulations are more easy to prescribe than to carry out. It becomes therefore the more important to prevent infection of the middle ear. The nose and nasopharynx should be cleansed with a warm solution of boric acid and borax, or other bland antiseptic fluid thrown into the nasal cavities by a spray or by a syringe very gently used. An antiseptic ointment, such as for example a weak eucalyptus ointment (ol. eucal. ℥v., vaselin ℥i.), should be applied to the mucous membranes with a camel's-hair brush after this cleansing process. When there is distinct evidence of pain in the ear, inflation should be practised only with the very greatest care and gentleness. Various palliative applications may be employed for the relief of pain; probably none is more effectual than the use of warm applications and the instillation of a few drops of a solution of cocaine and atropine in water (of each two or three per cent.). If other measures fail to give relief, or if inspection show that there is pus behind the tympanic membrane, it should be incised without delay. The child's head should be held firmly by an assistant, the membrane brought into view as fully as possible, and the puncture made in the lower and posterior part of the membrane. In many cases this operation gives immediate relief, in others there is no escape of pus for several hours, while in others again it must be repeated, for the wound heals rapidly, sometimes too rapidly. It should be borne in mind that otitis media may at any moment become complicated by mastoid suppuration with its well-known consequences, and that in any case the lymphatic glands below the ear are apt to be involved so that regard should be had to them throughout.

The treatment of measles during *pregnancy* does not call for special remark further than to say that tepid or cold baths are not contra-indicated if symptoms arise of such a nature as would under other circumstances render their use advisable. If miscarriage or premature delivery takes place, special care should be taken to prevent

septicæmia. Among the most important are to keep the woman in a room which is thoroughly ventilated and to insure local antisepsis of the parts.

Serum Therapy.—Several attempts have been made to employ a serum, derived from patients convalescent from measles, as a preventive or as a therapeutic measure. Thus H. Thompson inoculated nine children with fresh serum from small blisters raised on patients suffering from measles. The serum was inoculated at once by superficial scarification. One or two days later a slight "measly" eruption appeared about the scarifications; the eruption lasted two or three days and was accompanied by symptoms of slight catarrh. He believed that four of the children were thus rendered immune. Weisbecker used blood serum obtained from patients convalescent from measles as a therapeutic agent. He was careful to select patients free from all taint of organic disease, and in particular from syphilis. The serum was injected subcutaneously early in the attack in four cases. His results, for various reasons, appear to have been quite inconclusive, but he was himself convinced that the injections did good, and checked the development of bronchopneumonia. Hubert and Blumenthal have reported that the serum treatment, which they employed in nine cases of measles, shortened the duration of the disease and caused rapid disappearance of the general symptoms. The serum they used was prepared from blood taken from convalescents by adding an equal quantity of the physiological solution of sodium chloride, and chloroform in the proportion of one per cent., and then filtering twice through a Berkefeld filter. Marmorek has tested the value of antistreptococcic serum in the treatment of bronchopneumonia complicating measles without obtaining any results which could be called even encouraging.

Convalescence.

A child who has suffered a severe, or even a moderately severe attack of measles is often left in a condition in which nutrition long remains much depressed and the tendency is often increased by the anxiety of the parents who keep the child too much confined to the house. It should, on the contrary, be taken into the open air as much as possible. Children of the scrofulous diathesis or those who are left by measles in an anæmic condition with flabby tissues are generally benefited by a change of air from a city to a bracing locality. Those who have a family history pointing to a liability to pulmonary consumption require special care during convalescence, and if the attack of measles have occurred early in the winter season, a

residence in a warm and sunny climate for the remainder of the season is very desirable as a precautionary measure for the avoidance of catarrh and the establishment of the general health.

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GERMAN MEASLES

(RUBELLA).

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GERMAN MEASLES.

Name and Synonyms.—Among the names which have been given to this disease we find, according to Griffith, Rubeola, Rubeola sine catarrho, R. notha, R. epidemica, R. morbillosa, R. scarlatinosa, Rosania, Roseola, Roseola epidemica, Rubella, Rosalia, Rosalia idiopathica, Scarlatina morbillosa, Scarlatina hybrida, Morbilli scarlatinosi, Rötheln, Feuermasern, Roseole, Roseole idiopathique, Rubeole, Rougeole fausse, German measles, French measles, False measles, Bastard measles, Hybrid measles, Bastard scarlatina, etc.

The author agrees with Griffith that the term "rötheln" should never be used in this country, not because it is difficult to pronounce, but because it is not an English term. Furthermore, if a foreign term be used, we should always strive to use a term of a universal language, which in our profession is the Latin. If any English term is used, the term German measles might be made, as it is quickly being made, a universal designation.

History.

On account of the fact that so many different names have been given to this disease, historical research is more or less difficult, and leads to results not absolutely positive. It is more than probable that some of the old writers, especially the Arabian writers, knew of the disease, but it is comparatively recently that it has received its nosological position.

The history of German measles has been thoroughly compiled by Griffith, Edwards, and other authors. It may be divided into four periods, the first lasting up to the time when a definite separation was made between rubella and measles. While it is possible that Baillou in 1574 first gave a description of this disease as an independent entity, it is not until we come to the second period in the eighteenth century that we get positive information regarding its existence (De Bergen, von Orloff). More positive still are the descriptions given by Ziegler in 1784, Reil in 1790, and Fogel in 1792, which are accepted by Sprengel and Stark.

About 1812 Heim, who did so much work in connection with the

acute exanthematous diseases, tried to establish a differential diagnosis between measles, scarlatina, and rubella, but not very successfully.

We now come to the third period in the history of the disease, which lasted a considerable length of time; in that there were great doubts expressed regarding the independent nature of this disease. It is true that Henle in 1818 gave a very excellent description of the disease as a morbid entity, but in Germany, France, and England this period lasted until a comparatively short time ago. The views expressed at this time were either absolutely nugatory as to the independent existence of the disease, or else the authors were inclined to describe it as a hybrid affection, that is, a mixed form of scarlatina and measles. Even those great authors, Rilliet and Barthez, joined in the latter opinion. In the new edition, however, by Barthez and Sanné, German measles is accepted as an independent disease. But as early as 1857 Balfour, in England, and in 1852 Collins began to argue in favor of work for the specificity of rubella.

The great Hebra, of Vienna, can probably be looked upon as the most important antagonist to this view, and indeed, up to the time of his death, he—as does Kaposi at the present time—maintained that rubella cannot be looked upon as a specific entity. The reasons given are, first, that they have not seen this disease as a specific entity; but the second and principal reason can be found in their theorem that, everything else being equal, the same manifestations upon the skin are produced by the same cause. The latter reason is undoubtedly the cause of their adherence to the identity of variola and varicella.

As in the case of varicella, the principal opposition found in Vienna came from those who practised especially among children. In Berlin the great opposition to the acceptance of rubella as an individual disease came, and still comes, from the great master of pediatrics, Henoch. Gradually, however, the modern school of pediatrics, and with it the whole profession the world over relinquished the idea either that rubella is a fragmentary development of measles or of scarlatina, or that it is a hybrid disease; so that we see in Germany such authors as Thierfelder, Arnold, Wunderlich, Peltz, Oesterreich, v. Ziemssen, Thomas, Baginsky, Emminghaus, Rehn, Leube, indeed all those who have written text-books in later years, accept this modern view of the nature of rubella. In France, it is the modern school again which has accepted this same view—Sevestre, Juhel-Renoy, Comby, and a great many others.

After all, the great fight for the independence of the disease has come from the English-speaking people, such as Aitken, Moore,

Dyce Duckworth, Robinson, Cheadle, Squire, Tonge Smith, Ellis, Hague Brown, in England; and in this country J. Lewis Smith was probably the first to give great prominence to the disease (1872 to 1874), although Holmes of Boston, as early as 1843, and Cotting in 1853, had already given excellent descriptions of the disease. Then followed three most admirable articles by J. P. Crozer Griffith, Hardaway, and Atkinson and Edwards, the result of which has been to place the disease, in this country at least, upon a solid foundation as to its position among the other acute exanthemata. The author is very largely indebted to these articles for his references to the literature, and for much other information.

It has seemed to the writer that in order to establish the independence of rubella as a morbid entity, it would be necessary to prove the following propositions:

1st. That it is due to a specific poison.

2d. That the disease has an average clinical picture.

3d. That by contagion or infection it produces only its like.

4th. That the disease renders the patient immune to rubella, and to nothing else.

As to the first, as in all diseases, the proof is absolutely wanting, but it will be remembered that this is the case up to the present with all the acute exanthemata, and yet nobody denies the specific nature of measles, scarlatina, or varicella, the latter, possibly with the exception of the members of the Viennese dermatological school; so that up to the present time the absence of this proof means as little against rubella as it does against the other diseases mentioned.

As to the second, this can be considered as distinctly proven, in that rubella in some way or other differs from the other exanthemata in the average of all the various stages of the disease—*i.e.*, period of incubation, prodromal period, period of eruption, and period of decline.

Townsend, in opposition to this, has drawn conclusions "very unsatisfactory, it is true," he says, referring especially to individual cases, one of his conclusions being "that the symptomatology of rötheln is not distinct from that of measles, and that it is therefore impossible to make a diagnosis from a single case."

While this may be admitted for individual cases, the average symptomatology—both for individuals and epidemics—is so thoroughly established that, taking into consideration that which follows under propositions three and four, difficulty in diagnosis is certainly an exceptional occurrence. This, however, can just as well be claimed for the other acute exanthematous diseases. Thus individual cases of scarlatina occur in which it is almost impossible to make a differential diagnosis. All the first cases at the beginning of a small-

pox epidemic present the same difficulties as a rule, so that this objection cannot hold good as to the non-specificity of rubella.

The third proposition is most positively proven by the occurrence of the disease in epidemics—in other words, that this disease produces its like. While in certain epidemics of scarlatina, measles, and smallpox we may have abortive forms of either one or the other of these diseases, no one has ever claimed to have seen an epidemic in which there is constantly as wide a difference between the various cases as there is in an epidemic of rubella, between rubella and scarlatina on the one hand, or measles on the other. Nor is it likely that all the cases in any epidemic would represent abortive types of one or the other of the acute exanthemata.

As to the fourth proposition, in regard to the immunizing properties of an attack of rubella, quotations from almost every author who has written on this subject would suffice to show the truth of this proposition.

As to the reasoning of Hebra in favor of the identity of rubella and measles, but especially of variola and varicella, an occurrence may be related which happened while the author was going through the wards of the dermatological service with this great master. A child was brought to the station with varicella, and as was this master's custom, placed in the smallpox ward. In about two weeks after being received in this ward this child was attacked with variola. Upon being questioned by the writer as to his explanation for this occurrence, Hebra stated that second attacks of acute exanthematous disease were by no means uncommon; and yet, if it were true that rubella represented a second attack of measles or of scarlatina, this occurrence would be almost the rule and not the exception, for in the vast majority of cases the patients with rubella have certainly had measles and very often scarlatina. The author has repeatedly seen patients who had had both diseases and yet have been attacked by rubella. Any number of observations of this sort are on record, a most interesting paper having been written on this subject by the assistant of Kassowitz, v. Genser, in 1888.

Morbidity.

It is undoubtedly true that, as in all of the acute exanthematous diseases, childhood is the period of life that suffers most. But with the exception of variola, possibly no disease of this class so frequently affects adults. In the author's experience, more physicians have been attacked by this disease than by all the other exanthematous diseases taken together.

Etiology.

We know nothing concerning the ultimate cause of this disease. Certain investigations made by Klamann and Edwards go to show that here also there are lower forms of life which may be found in the blood, especially in the liquor sanguinis; but nothing goes to show that these are connected with the prime cause of the disease. Like all other diseases belonging to its class, it may be carried by direct or indirect contact with the patient; it may be transmitted by bedding, clothing, even by entering the room in which the patient had been confined. According to the author's experience, the disease is highly contagious, possibly not so much so as measles, but certainly approximating it. This question is a difficult one to solve in connection with the exanthematous diseases, as the morbidity has not as yet been thoroughly established.

Symptoms.

Period of Incubation.

A number of authors have made observations with the following results. The list does not claim to be complete, but will give an idea of that which is the essential peculiarity of the disease, namely, the extreme variability of this period. This point has already been dwelt upon by Griffith.

Atkinson	14 to 21 days.	Griffith	5 to 11 days
Boudet	12 to 14 "	Hardaway	Longer than measles.
Bourneville	8 "	Hatfield	10 days.
Bricon	8 to 10 "	Jacobi	14 to 21 "
Clausen	17 to 20 "	Longstet	18 "
Cuomo	17 days, never less.	Pollock	6 to 16 "
Cotting	8 weeks.	Juhel-Renoy	15 "
Cheadle	15 days.	Robinson	6 to 7 "
Duke	15 to 16 "	J. L. Smith	7 to 21 "
Duckworth	16 "	Scholl	5 to 21 "
Earle	17 to 21 "	Squire	8 to 21 "
Edwards	10 to 12 "	Steiner	10 to 14 "
Eichhorst	14 to 21 "	Tonge Smith	14 "
Glaister	4 to 5 " or longer.	Vacher	13 "

Didier states that it is longer than in measles and much longer than in scarlatina.

From this table it will be seen that the shortest period of incubation is five days, and the longest twenty-one days. Some authors have apparently had the same result in all their cases, Cheadle, Cotting, and Cuomo; while, on the other hand, we find excellent

observers, like Griffith, finding a very short period of incubation in some cases. The writer's experience agrees with that of Hardaway, that the period of incubation is longer than that of measles. But at all events it can be stated that in none of the acute exanthematous diseases is the period of incubation so variable, and therefore so characteristic, as it seems to be in the various epidemics of rubella that have been reported. In none of the diseases does such a latitude exist as in the statements above quoted.

Period of Invasion.

This period differs according to the subject attacked by the disease. As a rule it is not at all marked. When it is, it may last from twelve to twenty-four hours. Usually the first evidence of marked illness is the appearance of the eruption; exceptionally, in private practice, in very irritable, neurotic children, we find that it may last longer and that there are pronounced symptoms to be described hereafter which call attention to the illness of the child. Under ordinary circumstances, exaggerated in the children just mentioned, symptoms referable to the mucous membrane of the respiratory tract may be complained of—coryza, cough, injection of the eyes, sore throat, sometimes slight epistaxis; at other times the disease begins with symptoms on the part of the gastrointestinal tract—vomiting, more or less diarrhœa, or constipation. Not infrequently we find a combination of these symptoms, and then we have, as will be seen hereafter, a clinical picture that may be suggestive, especially in the presence of an epidemic, of what is to come.

As a rule this period is afebrile. Enanthem there is none.

Period of Eruption.

The eruption begins on the face, as a rule. It extends in twenty-four hours to the feet. It is a more or less discrete, punctated, macular eruption in the beginning, surrounded by hyperæmia, somewhat elevated, of a distinct red color, the centre being most highly colored. Filatow and Musser describe a rubella scarlatinosa, and a rubella morbillosa. The present author is inclined to agree with these writers, in that he has seen epidemics in which the scarlatiniform nature of the eruption has been best marked, and others in which the type was that of measles. It is not an infrequent occurrence to have both types represented in the same individual at the same time. Indeed, this might be looked upon as a characteristic of the disease, and as giving rise to the views expressed before by various authors of the hybrid nature of the disease. But the eruption of scarlatina differs

from that of the German measles, first, as to color, which never is so bright in the latter as in the former; secondly, as to the place of origin, which is always upon the face; and thirdly, as to the time of maturation of the eruption, which is extremely short. From measles the eruption may be distinguished by the circinate appearance of the former; by the tint, which is always bluish in measles; and, again, by the time of complete florition. In German measles the eruption is developed over all parts of the body; not infrequently found even upon the soles of the feet and the palms of the hands, as in scarlatina. It has been noted that where pressure is applied there the eruption is strongest developed, depending undoubtedly upon the fact that the rash is due to a hyperæmia of the skin. It attains its maximum development in a very short time, and for this reason the polymorphism of the eruption is so characteristic a symptom of this disease, just as in varicella, except that upon the same places of the body we are apt to have the same external manifestation. The rash lasts not to exceed five days in all. The external manifestations develop in about three days, depending upon the nature of the epidemic; not that more intense epidemics produce a longer duration, but that simply the character of the epidemic seems to establish a rule in this respect.

Anomalous developments of the rash are not uncommon. It may begin first upon the chest, and then extend upwards and downwards, or it may develop upon the trunk or the limbs, and then not extend, so that we may speak of a rudimentary form of German measles.

The characteristic enanthem is easily overlooked, indeed its occurrence is denied by most authors. It appears simultaneously with the exanthem, becoming evident about six hours after the first symptoms and lasting not to exceed twelve to fourteen hours. It occurs on the soft palate, sometimes extending over on to the hard palate, and is marked by the appearance of small, discrete, dark red, but not dusky, papules which disappear in a short time, leaving no traces behind. The rest of the mouth may or may not be congested; the tonsils are more or less affected according to the nature of the epidemic.

The tongue may have a white coating, depending upon the gastrointestinal condition; but we never have tumefaction and hyperæmia of the fungiform papillæ, and we never have the characteristic strawberry tongue of scarlatina. Again, various authors have made the statement that the latter does occur in German measles. The author, in an extensive experience, has never seen it; and indeed, relies upon this evidence as one of the most important differential signs between scarlatina and German measles.

One of the most common symptoms present is tumefaction of the lymphatic glands at the angle of the jaw, the anterior cervical glands,

and not infrequently submaxillary glands—all of which may be painful upon pressure. While this condition does not exist in every case, it may be looked upon as a very valuable aid in the diagnosis of this disease.

The temperature may be normal, or nearly so, throughout the course of the disease; at all events, there is no characteristic temperature curve for German measles. Exceptionally high temperatures to 105° F. have been noted; but such an occurrence is extremely rare, and may possibly be due to some complication.

On the part of the respiratory tract we may have evidences of laryngitis, laryngotracheitis, or bronchitis. In the majority of cases either form of trouble develops but slightly. The tonsils are always enlarged. There is more or less catarrhal angina. Not infrequently a further development takes place, in that the lacunæ are filled up by exudation, presenting more or less well-pronounced evidence of a follicular angina.

Period of Desquamation.

In the great majority of cases there is no desquamation at all. When this does occur, it may be furfuraceous or lamellar; again, partaking of the nature of the desquamation of either scarlatina or measles. This passes away in a very short time, from two to five days, and leaves the skin in a perfectly healthy condition. In the large number of cases that have been reported by Edwards, desquamation was present in the form of furfuraceous scales in every case. This was certainly an exceptional epidemic, as the statement made above must be looked upon as the rule and not the exception. Edwards noticed not infrequently "a delicate brownish-yellow pigmentation. This coloring did not appear to bear any relation to the color of the eruption, or its severity." This pigmentation has also been noticed by a great number of others. It is very short-lived, and as a rule escapes detection. The urine presents evidences of a febrile condition. Under normal circumstances nothing more is found. The author is inclined to agree with Hardaway, who claims that albuminuria is an anomalous symptom, giving rise to doubt in diagnosis. Certainly, when it does occur, it must be looked upon as a complication.

Diagnosis.

In an individual case the differential diagnosis may become very difficult, and this undoubtedly has given rise to the views expressed in regard to the non-existence of German measles as an individual

disease. In the presence of an epidemic such a difficulty does not exist because it would be extremely unlikely that we should have a large number of cases in which the symptoms described as fairly characteristic could be observed. The diseases for which German measles can be mistaken are measles, scarlatina, and, in the author's experience, influenza. In the epidemic of influenza of 1892 very many cases were observed by the author in which a differential diagnosis between scarlatina, German measles, and influenza proved difficult in the beginning. After the cases began to increase in number the differential diagnosis seemed easier.

The following table, which has been modified from Griffiths and Edwards, may prove of value:

TABLE OF DIFFERENTIAL DIAGNOSIS.

Rubella.	Measles.	Scarlatina.	Influenza.
		Incubation.	
Very variable; from five to seven to twenty-one days.	Fourteen days.....	One to seven days.....	Seven days.
		Prodromal Symptoms.	
Absent, or from twelve to twenty-four hours.	Usually last three days.	Twenty-four hours or less.	Absent; sudden appearance of symptoms.
Catarrhal symptoms slightly marked.	Severe catarrhal symptoms of nose and eyes, also respiratory apparatus; enanthem characteristic. Blue mouth and tongue.	....	Catarrhal symptoms; gastrointestinal or nervous symptoms present.
Sore throat common; enanthem lasting only for hours, on soft palate.	Sore throat rare; occasionally observed.	Marked sore throat, with characteristic enanthem.	Sore throat may be present or absent; no enanthem.
Vomiting rare.....	Occasional vomiting ..	Vomiting the rule.....	Vomiting absent except in the gastrointestinal type.
Fever absent or slight..	Characteristic temperature curve.	High fever and pulse out of proportion to temperature.	Temperature sometimes high; sometimes intensely high; sometimes not especially marked.
Enlarged glands; usually well marked.	Enlarged glands, as in all acute exanthemata; not characteristic.	Enlarged glands as usual in acute exanthemata.	Glandular enlargement absent, except as result of special complications.
		Eruption.	
First on face	First on face	First on chest and neck.	May develop anywhere on the body; no regularity.
Spreads very rapidly, either fading from one part before in full bloom on another; or covering entire body in twenty-four hours.	Gradually spreads over body; maximum on third day.	Spreads slowly; maximum on fifth day.	May not spread at all; localized to one place; but sometimes spreads very rapidly all over body.
Lasts three to four days or less.	Lasts on average four days.	May last five to seven days or more; sometimes less.	Usually lasts two to four days.
Color usually pale red...	Color purplish.....	Color intensely red.....	Color depends upon nature of eruption.
More or less elevated; not arranged in groups as in measles; spots smaller; no small red points as in scarlatina.	Irregular, crescentic grouping of papules.	Minute red points; confluent.	Erythematous eruption; urticaria; herpes; or hemorrhagic forms.

TABLE OF DIFFERENTIAL DIAGNOSIS.—*Continued.*

Rubella.	Measles.	Scarlatina.	Influenza.
		Symptoms of Eruptive Stage.	
Slight catarrhal symptoms.	Severe catarrhal symptoms.	Coryza absent except in bad cases.	Coryza present.
Slight sore throat.....	Sore throat uncommon.	Sore throat always present in a marked way.	Sore throat in some epidemics well marked.
Enlargement of glands, especially cervicals.	Usually enlargement of glands as in acute exanthemata.	Glands at angle of jaw especially enlarged frequently; not uncommonly glands in other parts enlarged.	Glands enlarged as described before.
Tongue not characteristic; no strawberry tongue.	Complete development of the bluish tongue.	Tongue characteristic strawberry development.	No characteristic tongue.
Fever absent; or if present no characteristic temperature curve.	Characteristic temperature.	Temperature usually high according to the characteristic temperature curve.	Temperature not affected by eruption.
Pulse in proportion to fever.	Pulse in proportion to fever.	Pulse out of proportion to temperature.	Pulse not abnormal.
Albuminuria exceedingly rare.	Albuminuria very uncommon.	Albuminuria not uncommon.	No albuminuria.
		Desquamation.	
Absent, or slight and branny.	Branny.....	Lamellar.....	Desquamation as in mild forms of dermatitis.

Complications.

These always depend upon secondary infections, as is the case with the other exanthemata as a rule. The most common seat of complications is to be found in the respiratory tract, but even this is rare. Thus, in Griffith's one hundred and fifty cases, only two had pneumonia. Occasionally we find inflammations in other divisions—severe bronchitis, pleuritis. The lesions of the upper part of the respiratory tract have already been referred to as normal conditions in the disease. Complications on the part of the gastrointestinal tract occur not infrequently—enteritis, enterocolitis, gastroenteritis. These are to be looked upon as complications only when developed to an abnormal extent. Troubles in the mouth are not uncommon. The ordinary stomatitis catarrhalis has already been referred to. Stomatitis aphthosa in some epidemics occurs frequently, depending in all probability upon complication with streptococcus infection. Complications on the part of the skin occur occasionally in the form of furunculosis, sometimes erysipelas, occasionally erythematous eruptions or urticaria. Febrile œdema has been noted in several instances. On the part of the organs of special sense, catarrhal troubles of the eyes—blepharitis, conjunctivitis. On the part of the ear, otorrhœa has been noted. Endocarditis has been observed as well as rheumatism and nephritis. Judging by the statements made

by various authors, certain other diseases are apt to follow German measles—thus diphtheria, mumps, abscesses of lymphatic glands; but the author has had no experience with these cases. It is stated that there is a relapsing form of this disease. In all his experience the author has never seen a single case of relapse.

Prognosis.

The prognosis is absolutely good. This certainly holds for private practice. Edwards, Hatfield, and a large number of other authors have reported deaths; but the majority of observers agree with the statement made above that the prognosis is favorable. Even Edwards states that in private practice he has never seen a fatal case. While exceptionally in a weak, puny, highly receptive child a complication may occur that will end fatally, upon the whole, with good sanitary surroundings, the disease runs its course absolutely favorably. For cases in private practice the statement might be made that the chances of a serious complication occurring during German measles are the same as they would be in health. In the greatly neglected, exposed, underfed children, as we see them in hospital practice, this may not be true; but even here the writer's experience has been much more favorable than the reports of other authors would indicate. In all the cases that have come under the observation of the writer, but one has terminated fatally, and death in that case was due to nephritis.

Treatment.

Prophylaxis.

On account of the mildness of this disease, the writer has never found it necessary to take any measures as to prophylaxis. It is a grave matter of doubt with him whether such action is necessary; certainly not in private practice. We do not guard especially against chickenpox; why should we guard against a disease in which the mortality is equally small? In hospital practice, prophylaxis may be called for, and in the presence of a severe epidemic should be carried into effect. Here all the measures recommended under the head of prophylaxis in the article on Scarlet Fever should be adopted; more, however, the author is willing to confess, on account of the unfavorable reports given by such reliable authors as Edwards, Hatfield, and others than on account of his own experience. The patient should be kept isolated for two weeks, certainly until desquamation has been thoroughly completed.

Medical Treatment.

The treatment can only be symptomatic. Asepsis of the mouth, referred to in the article on Scarlet Fever, should be carried out in order to prevent complications. Gastrointestinal symptoms may require special attention. Diseases of the respiratory tract must be treated according to the rules laid down in other parts of this work. We have no specific medication, and therefore no especial recommendation can be made. At the termination of the disease the patient should be bathed thoroughly, his hair being disinfected, and he should then be allowed to go out as if he had not been ill.

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CHICKENPOX.

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CHICKENPOX.

Definition.—Chickenpox or varicella is an acute infectious disease peculiar to infants and children. It is accompanied by only slight fever and other constitutional symptoms. The most prominent feature of the disease is the characteristic vesicular eruption on the skin. Papules may appear in the beginning, but they disappear very quickly, often in an hour or two, and they are not characteristic. Pustules never or rarely appear, and then only when there is a mixed infection. The eruption may also be seen on the mucous membrane of the mouth and throat, and more rarely on that of the nose, larynx, and prepuce or vagina.

History.

The early history of varicella is inseparably connected with that of variola, although certain early descriptions leave no doubt that it was known in olden times. It first appeared under the title of crystalli, and the names that have since been applied to it are innumerable, but most of them are based upon its resemblance to smallpox. Until the early part of the seventeenth century, when inoculation against smallpox was introduced, varicella, on account of its mildness, received very little study. The opponents to inoculation based one of their strongest arguments against this method on the fact that inoculation did not protect against varicella, which they considered a modified or mild type of variola. As a result of these arguments a more careful study of varicella was undertaken by Willan, Heim, and others, which resulted in demonstrating beyond doubt that varicella is a distinct specific disease and not a modified or mild type of variola.

After Jenner had introduced vaccination in 1796, cases of varioloid began to appear. These cases resembled varicella so closely that the opinions of medical men were again divided, and even to-day there are many who believe in the identity of varicella and variola. The most prominent advocates of this view are Hebra and the Vienna school.

In spite, however, of these authorities, there can be no doubt

that chickenpox is an independent and specific disease, and not a mild or a modified type of smallpox. This is proven conclusively by many facts: Vaccination does not protect against varicella; varicella always produces in those exposed to its contagion varicella and never variola; epidemics of varicella rarely or never occur in connection with cases of variola; there are no cases on record of congenital varicella, but variola of the unborn child is not unknown; in most cases negative results are obtained from the inoculation of the contents of the varicella vesicles, although the ease with which this disease spreads and carries infection is very great; and, finally, the character of an epidemic of the two diseases is quite different.

Steiner's inoculation experiments are especially interesting. He obtained positive results from inoculation with the contents of the vesicle of varicella, although Thomas and others had inoculated without success. He took the clear, transparent lymph from the vesicles, and with it inoculated two children in two different families. In the first case the lymph was used as in the ordinary vaccination against smallpox. No signs appeared until four days, when the child became slightly feverish and restless. This continued with more or less severity until the eighth day, when an eruption of vesicles developed, and the child suffered from an eruptive disease which seemed to run the typical course of varicella. The second case ran almost an identical course: marked prodromal symptoms, redness of mouth and throat from the appearance of the eruption, which was on the eighth day after inoculation, etc.

Steiner concludes, from a study of eight successful cases, that it is possible to produce varicella by inoculation with the contents of the vesicle (eight cases out of ten were positive); that varicella is always produced, never variola; that the period of incubation is eight days; that in the eight successful cases, prodromal symptoms were present in four cases and absent in four cases; that the height of the fever corresponds to the time of the appearance of the first eruption; that, as a rule, the fever does not rise with the appearance of each fresh crop of vesicles; and, finally, that vaccination does not protect against varicella and neither does varicella protect against variola.

Etiology.

Varicella is very contagious and, although it is undoubtedly due to a specific germ, this has never been isolated. Various microorganisms have been found in the contents of the vesicles, but there is no evidence that any one of these bears an etiological relation to this eruptive fever.

It is not uncommon to have secondary infections in varicella, and the disease may be complicated with scarlet fever, measles, and other eruptive diseases in which the skin manifestations are prominent features. Again, the vesicle itself may be the entrance for some secondary infection. To this class belong the so-called gangrenous forms of chickenpox and the secondary infections due to staphylococci, streptococci, etc., reported by Steiner, Brunner, Braquehaye, and others.

Symptoms and Diagnosis.

Varicella has an *incubation period* of about two weeks after exposure, but, when the disease is given to the patient by inoculation, the first symptoms always appear in eight days, which is probably the true incubation period. There are never or very rarely during this period any of the prodromal symptoms, such as lassitude, headache, fever, chills, etc., so often seen in the other infectious diseases.

The vesicle is usually the first symptom noticed, but occasionally a small, round, non-elevated, hyperæmic spot may be observed a few minutes, rarely more than a few hours, before the vesicle appears. There are certain rare cases in which this hyperæmic roseola disappears without the formation of the vesicle. Here the diagnosis is very difficult and must be made by exclusion. Diagnostic points of value in these cases are the history of exposure to infection and the presence of a characteristic round roseola, which is slightly or not at all elevated and which disappears very quickly.

In a few very mild cases with only a slight exanthem, fever may be absent during the whole course of the attack. In most cases there is a slight rise of temperature of one to two degrees above the normal. This fever rarely or never begins before the appearance of the eruption, and it lasts in most cases from three to four days, although it may run a shorter or a slightly longer course. The fever in complicated cases due to secondary infection may be severe. Its character depends entirely upon the character of the mixed infection.

In the early stage of chickenpox the exanthem is very characteristic, and a mistake in diagnosis can hardly be made even by a superficial observer. Later in the course of the disease, especially after the vesicles have become broken and a mixed infection has taken place from scratching and other outside sources, there may be some difficulty in determining the exact character of the lesion. It should not be forgotten that it may be associated with other infectious diseases, and cases have been reported in which the varicella patient suffered at the same time from smallpox, measles, or scarlet fever.

The characteristic eruption consists of vesicles, varying in number

from a dozen to several hundred, and varying in size from a bead to a large pea. These vesicles are mostly round and discrete, are seated very superficially, and developed upon a flat and slightly hyperæmic roseola. Very characteristic groups of small discrete vesicles are often found upon single parts of the body, but large single ones are always found in the neighborhood of these groups. One very marked feature of the eruption is the successive crops of lesions, so that different stages are found at the same time and in close proximity. This is one of the most valuable diagnostic points in excluding variola.

The eruption on the mucous membrane gives a very characteristic appearance. Vesicles form, which quickly lose their delicate covering and then resemble aphthous ulcers, with a well-marked red zone surrounding them. They are most abundant upon the hard or soft palate, but may appear on the mucous membrane of the nose, the larynx, the prepuce, or the vagina. Marfan and Halle describe two cases in which the larynx was involved.

The first case was that of a boy three years of age. He was suddenly seized with great difficulty of breathing and fits of suffocation. Inspection of the oral cavity, together with a bacteriological examination, gave no evidence of diphtheria. On account of the cyanosis, tracheotomy was performed. There was no membrane. After an injection of diphtheria antitoxin, the typical eruption of varicella appeared on the forehead, neck, cheeks, abdomen, and back. The same eruption appeared on the body of a younger brother of the patient. After a little while the breathing became normal and recovery supervened.

The second case was that of a child nine months old. The typical eruption was distributed over the greater surface of the body. There was marked stridor with difficulty of breathing. Examination as to the presence of diphtheria was negative. Nevertheless, an injection of 20 c.c. of diphtheria antitoxin was given. Bronchopneumonia and copious diarrhœa followed, and death was not long delayed. The post-mortem examination revealed a circular, shallow ulceration on the posterior part of the right vocal cord, about the size of a pea (a burst varicella vesicle).

The prognosis of laryngeal varicella is extremely dubious. As yet, statistics furnish but one recovery. Treatment consists in either intubation or tracheotomy. Stenosis of the larynx in varicella may at times be confounded with diphtheria. A bacteriological examination will serve to distinguish the two.

The eruption begins to decline in a few days. Some of the vesicles become flaccid or apparently slightly umbilicated from the absorption of their contents, and others rupture, either spontaneously or from scratching. They finally dry up and the crusts drop off,

leaving small circular marks which shortly disappear. However, in delicate skins or after severe lesions, the scars may persist.

The *differential diagnosis* is rarely difficult. Herpes zoster and vaccina are always easily excluded, if the case is carefully examined. If the disease is complicated with pemphigus, measles, smallpox, scarlet fever, etc., the diagnosis becomes very obscure and in many cases impossible to make out clearly in the beginning.

Variola is practically the only disease with which there is much chance of confounding varicella. If we remember their characteristic features we will rarely or never be troubled. Varicella is quick in developing, has no or only slight prodromal symptoms, has no backache, and runs a rapid and mild course. Variola, on the other hand, is essentially slow in developing, has marked and severe prodromal symptoms, has an intense backache, and runs a slow (two to three weeks) and a severe course. The vesicles in varicella are soft to the touch, different stages of the lesions are usually in close proximity at the same time, the vesicles rarely leave scars and rarely become pustules, and the eruption is usually very abundant. In variola, the eruption feels shotty to the touch, the lesions in close proximity are always at the same stage of development, the vesicles commonly become pustular and umbilicated, and scars are usually left.

The so-called *gangrenous varicella* is undoubtedly a chickenpox complicated with another infection, and certainly does not deserve a separate classification.

One of Griffith's cases was especially interesting. The patient was twenty-two months old and during convalescence from pneumonia developed a diphtheria of the tonsils, and four days later measles with a temperature of 104° F. Three days after the measles first showed itself on the skin, the varicella appeared. The eruption speedily changed from vesicles to bullæ. These latter increased rapidly in size and ruptured, leaving an erythematous area, around which appeared cup-shaped excavated ulcers with ragged edges. Some of these ulcers discharged an ichorous pus and others were covered with a dark-brown crust. The child died and the autopsy showed the presence of diphtheritic membrane in the trachea.

Many other cases of gangrenous varicella are reported, notably by Abercrombie, Howard, Hutchinson, Payne, Woodward, Büchler, Andrew, Stainforth, Demme, and Spivak.

Steiner reports a case of secondary infection, the symptoms of which began after the varicella had progressed favorably for six days. There was a high temperature, some vomiting, and later a convulsion, and pain on moving the right leg. The unfavorable symptoms rapidly increased: high fever, small and rapid pulse, somnolence, loss of appetite, trismus, and slight twitchings of the muscles. The

swelling of the leg became more marked, until finally the entire thigh was involved and the skin and soft parts of the upper half of the thigh were much infiltrated. The diagnosis of acute osteomyelitis of the femur was made, and the post-mortem examination showed that the upper third of the femur was bared of periosteum and bathed in pus, and that the muscles of the thigh were infiltrated with a seropurulent exudate.

Brunner, Bolognini, and others, report cases in which there was an acute staphylococcus infection; Girode and Braquehaye cases of streptococcus infection; and many cases are reported in which the disease was complicated by one of the other infectious diseases, such as measles (Foster, Comby, Nash, Szczypiorski), scarlet fever (Alezais, Ayer, Tordeus, Galhard, Snell, Comby), variola (McCollom, McVail), and tuberculosis of the skin (Feulard).

In Brunner's case the patient had, during an attack of varicella, an acute suppurative inflammation of the periarticular tissues of the elbow-joint, due to a staphylococcus infection. The humerus in the region of the supratrochlear fossa and of the inner condyle was denuded of periosteum. In spite of an operation which evacuated the pus and drained the abscess cavity the temperature continued high, the child was apathetic, there was albumin in the urine, and finally there developed a double parotitis and an abscess of the left middle ear. The child died on the ninth day, and the post-mortem examination showed the presence of pus in the anterior mediastinum, the pericardium, the bronchi, the spleen, and the kidneys; and this pus as well as the blood showed the presence of staphylococcus pyogenes aureus. This organism was also obtained in pure culture during life from the pus, the blood, the urine, and the perspiration of the patient. The infection was undoubtedly secondary to the varicella and the invasion took place through the varicella lesions.

Löhr reports two fatal cases of varicella, one due to a mixed infection with the staphylococcus pyogenes aureus and the other to a general miliary tuberculosis.

Braquehaye's case was apparently taking the normal course of varicella until the ninth day when the temperature suddenly rose, and during the next two days a purulent arthritis of the knee and of the elbow appeared. The joints were opened and the pus showed the presence of numerous streptococci. The patient died twenty days after the onset of the varicella and the post-mortem showed, in addition to the arthritis, a septic endocarditis, and numerous cocci were found in the liver.

That varicella should be complicated with the other infectious diseases would be expected. The chief interest in these cases is that of diagnosis, especially when the complicating disease is one in which there are skin lesions. However, there is little difficulty in making a diagnosis, although confusion may result between scarlet fever and

the rash which sometimes appears in certain cases of varicella. The diagnosis from scarlet fever rests upon the absence of the angina and peculiar tongue and upon the sudden appearance and short duration of the rash. The appearance of the rash is usually accompanied by a rise of temperature and an aggravation of the general symptoms. Its disappearance is not followed by desquamation. Occasionally the rash may resemble the eruption of measles instead of scarlet fever (Chauffard), but this occurs very seldom.

Sequelæ, Prognosis.

Chickenpox runs such a mild course that the physician is rarely called to see cases, outside of institutions, even for diagnosis. The prognosis is nearly always favorable and the sequelæ are seldom dangerous.

When the outcome of the case is bad it is almost uniformly due to a complication from some outside source, as pneumonia, gangrene, etc., or with one of the other infectious diseases, as variola, measles, diphtheria, scarlet fever, etc.

The most common consequence of varicella is a mild type of anæmia which readily yields to simple treatment. However, it should not be forgotten that chickenpox, like all the infectious diseases, may be followed by a serious parenchymatous nephritis, and also that, if the lesions of the skin and mucous membrane are not properly taken care of, they may afford an entrance for some serious secondary infection with the tubercle bacillus, streptococcus, staphylococcus, etc.

Undoubtedly the most serious sequelæ of varicella are nephritis and the infections through the lesions of the skin. In the kidney cases, the urine contains albumin and casts, and the usual symptoms of a parenchymatous nephritis are present. Although this is not a frequent complication, cases have been reported by Henoch, Janssen, Nuger, Oppenheim, Schwab, and others. It usually runs an acute course, and the patients make a rapid and good recovery. However, fatal cases have been reported, and the writer has seen one case in which the disease of the kidney after a mild attack of varicella ran a chronic course, and after nearly ten years was the cause of the boy's death.

Treatment.

In most cases of varicella the treatment is purely expectant, for the constitutional symptoms are so mild that there is no danger. The child, however, should be isolated, especially in institutions. It

should be kept in bed in a well-ventilated, sunny room at an even temperature. The diet should be liquid. The irritation of the skin should be allayed as much as possible with a weak carbolic wash to avoid scratching and thus prevent scars. The skin should be kept active and the bowels free to relieve as much as possible the kidneys and to assist in the elimination of the poison. The urine should always be examined, and the child should remain under treatment until this excretion becomes normal. A parenchymatous nephritis may follow this disease, and I have seen two cases in which it became chronic and finally ended in death. The need of closely watching the kidneys in all the infectious diseases cannot be insisted upon too strongly.

Another source of danger is found in the lesions which follow this eruption. If they are not kept clean and properly dressed with some simple antiseptic ointment or wash, they allow infection from outside. One of the most serious sequelæ from this cause is an enlargement of the neighboring glands or even tuberculosis.

The anæmia, which is the usual result of this disease, can best be treated by a proper diet, good care of the skin, and plenty of fresh air. A good iron preparation, such as ferratin or saccharated carbonate of iron, may be of great service.

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GLANDULAR FEVER.

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GLANDULAR FEVER.

GLANDULAR fever is an acute infectious fever without exanthem, characterized by adenitis affecting especially the anterior cervical glands.

History.

The first detailed description of this disease as an infectious epidemic disorder, under the name of *Drüsenfieber*, was given by E. Pfeiffer,[1] in 1889—though, according to Protassow,[2] it had been described by Filatow, of Moscow, at an earlier date. It has since been recognized by Heubner,[3] von Starck,[4] Hoerschelmann,[5] Hesse,[6] and others in Germany; by Moussous,[7] in France; by the present writer, Donkin,[8] Coutts,[9] and Fisher,[10] in England; and in America by J. Park West,[11] who has given an excellent description of the most widespread epidemic hitherto recorded.

Pathology.

The disease occurs usually in small epidemics limited to a single family or household, but affecting as a rule all or nearly all the members of the household under the age of about fourteen years. Adults seldom suffer, but during an epidemic a few cases may occur among them. The lymphatic glands most constantly involved are those beneath and towards the front of the sternomastoid muscle. The adenitis as a rule occurs first on one side of the neck, usually the left, and then on the other. The posterior cervical and inguinal glands also may be affected, and in some cases the mesenteric. No local condition is discoverable sufficient to account for the adenitis. Pharyngitis and tonsillitis may be and as a rule are entirely absent, and when present the lesion is usually slight or chronic. The adenitis therefore appears to be the primary lesion, although it is probable that the infective agent finds entrance through the mucous membrane of the alimentary tract. The early infection of the anterior cervical lymphatic glands appears to render it probable that the infection finds its point of entrance through either the tonsils or the pharyngeal mucous membrane. The fact, however, that constipation is the

rule led von Starck to suggest that the primary seat of the infection was the small intestine, and Koplik has pointed out that if this were so the earlier affection of the glands on the left than on the right side of the neck might be due to the passage of the infective agent from the thoracic duct near its termination to the cervical glands on the left side. That an infective microbe may traverse the tonsils or the intestinal mucous membrane without producing obvious lesions in those structures, and yet cause a specific process in the related lymphatic glands with subsequent systemic infection, appears to be proved by the behavior of the tubercle bacillus in some cases, especially in children.

Cantlie[15] became familiar in Hong-Kong in 1891, and therefore before the outbreak of plague (which occurred in 1894), with an idiopathic glandular enlargement occurring in children in an epidemic form. The enlargement, he states, involved usually only one gland in the neck over the sternomastoid muscle, but at its anterior border. Apparently, therefore, the adenitis affected the superficial and not the deep cervical lymphatics, which are those usually affected in glandular fever. He mentions the occurrence of these cases in the course of a discussion of *pestis minor*, without, however, suggesting that they were examples of mild plague. It must be admitted that glandular fever does in the nature of its local lesion present a certain resemblance to the mildest form of bubonic plague (*pestis minor*). It is a curious fact, taken in conjunction with the extension of bubonic plague in the East since 1894, that it has been recognized in the far East for some years that a disorder characterized by enlargement of the lymphatic glands, usually those in the inguinal region, might occur in epidemic form both on board ship and in regiments ashore. Although it has only recently been described (by Godding[16]), many medical officers, both naval and military, appear to have been acquainted with the disorder under the name "non-venereal bubo." The glands usually affected are the inguinal, and Skinner[17] has suggested that as the "non-venereal bubos" in the cases he observed invariably occurred in the inguinal glands, and as the patients always had irregular action of the bowels, sometimes dysentery, and at other times apparently constipation, the enlargement of the inguinal glands may be due to secondary infection from the mesenteric lymph glands. The analogy between this theory of non-venereal bubo and that advanced by von Starck for glandular fever will be observed.

AGE.

As has been said, the disease is one which especially affects childhood, but infants are not infrequently affected, and in rare instances adults. Of Park West's ninety-six cases, the youngest was aged seven months, the oldest thirteen years. Few children exposed to the infection escape. In the epidemic described by the last-named writer, which prevailed in a sparsely populated district of Eastern Ohio, ninety-six cases occurred in forty-three families, and only twenty children belonging to these families escaped.

Symptoms.

No symptoms are noticed during the *incubation period*, which lasts usually six or seven days, though extremes of five and fifteen days are believed to occur.

The *onset* of the disease is sudden. The child begins to show signs of malaise. The neck is held stiffly, owing to the fact that movement causes pain; there is nausea, perhaps actual vomiting, the tongue is coated, the bowels are usually constipated, and the temperature is raised (101°–103° F.). There is in many cases abdominal pain, which only in a few, and those the mildest cases, ends in spontaneous evacuation of the bowels. Young children refuse food, and in older children complaint is made of pain or difficulty in swallowing, referred to the level of the cricoid cartilage. At an early stage there may be some tenderness in the anterior triangle, usually on the left side, but at this period the pain elicited by movement of the head is more conspicuous than that caused by palpation. Examination of the pharynx and tonsils may reveal no lesion or merely some chronic enlargement of the lymphatic tissues, so commonly observed, especially in town-bred children. In some cases there is undue redness from injection of the pharyngeal mucous membrane; only rarely distinct pharyngitis. In his ninety-six cases Park West observed transient injection of the pharynx in twenty-six cases, but pharyngitis in four only. The general symptoms are such as attend a moderate degree of fever, but are occasionally rather severe. Thus Fisher has observed delirium, and Moussous records a case in which the general aspect and condition of the patient were sufficiently serious to suggest the diagnosis of typhoid fever.

The *glandular enlargement* first becomes conspicuous on the second or third day of fever, and at about the same time the temperature attains its maximum (often about 104° F.). An elongated swelling is perceived beneath the sternomastoid muscle and towards its anterior

border. It is uniform to the eye, but on palpation is found to consist of three or four enlarged lymphatic glands, of which the largest is usually one which lies a little below the level of the angle of the jaw. The adenitis, which is in most cases observed first on the left side, attains its maximum on the second or third day, and then begins more slowly to subside. A termination in suppuration is not observed in uncomplicated cases. The pain on movement and the pressure on the surrounding parts cause the head to be carried stiffly, and in some cases it is flexed towards the affected side. The child dreads any handling of the neck or any pressure of clothes upon it. At or a little before the time when the enlargement of the glands attains its maximum, enlargement of the glands on the other side of the neck usually becomes perceptible and runs a similar course, though the degree of adenitis is commonly less severe. Other groups of glands may be successively involved, most often the post-cervical, but also the axillary and inguinal. Altogether, Park West observed enlargement in one or other of these three groups in three-fourths of his cases. In two cases in which the general symptoms were severe, Moussous observed the onset, on the third or fourth day of illness, of cough which occurred in paroxysms ending in vomiting, but without the characteristic whoop or glairy expectoration of whooping-cough. This appears to indicate that the tracheobronchial glands may be enlarged during the course of the illness. Much interest attaches to the enlargement of the mesenteric glands, which Park West observed in 38.5 per cent. of his cases. Pfeiffer recognized this occurrence in a large proportion of cases, but in very many patients it is not discoverable, although some abdominal uneasiness and tenderness is the rule. Enlargement of the spleen is perceptible in about half the cases, and in others there is tenderness in the splenic region. In almost all cases the liver is voluminous. In the milder cases there may be some looseness of the bowels from an early stage, but constipation is a characteristic of the disease; it is easily removed by purgatives, but in well-marked cases immediately recurs. The beginning of convalescence is in many, perhaps the majority, of the severer cases marked by the passage of thin greenish stools containing much mucus.

The fever and acute symptoms in cases of average severity last from five or six to ten days. The enlargement of particular groups of glands begins to diminish in from two to five days after they are first perceptibly swollen. By the successive affection of groups of glands the attack may be prolonged for two or three weeks. Park West noted an average duration of sixteen days, with extremes of nine and twenty-seven days. There is no rash, though in the early stage

there may be a dull-red flush of the face. When the enlargement of the cervical glands is established, it is more usual to see the face pale, with perhaps a little dusky congestion. The temperature curve is irregular. It generally attains its maximum on or about the third day, when the first group of glands to be affected are enlarging rapidly. It does not fall finally until the last group to be involved has begun to diminish. The pulse is rapid during the febrile stage, and often remains faster than natural for some days after defervescence has taken place.

Complications.

The list of complications is not long. Coryza, bronchitis, and other affections of the respiratory mucous membrane are not common and certainly form no part of the picture of the disease. Chapman[10] has recorded four cases of epistaxis among five children belonging to the same family. The most important complication is nephritis, which may be severe and attended by hæmaturia. Fisher has observed cases which led him to assert that transient synovitis is an occasional complication.

Convalescence.

After the fever has ceased the patient is left in a depressed condition, with marked anæmia. Occasionally the fever ends by an irregular crisis, with copious diarrhœa and abundant sweating. The enlargement of the glands subsides gradually, and they have generally ceased to be perceptible within ten days of defervescence, often much earlier. Diarrhœa, due apparently to chronic colitis, persists in some cases for a few weeks, but usually yields readily to suitable treatment. Restoration to health, however, is not complete in cases of average severity for one or two months.

Prognosis.

The disease is benign and complete recovery ensues in almost all cases, even in those in which the symptoms have been most severe, as well as in those in which nephritis occurs as a complication. Park West had only one death among his ninety-six cases, and the patient who succumbed was a delicate child convalescent from scarlet fever.

Diagnosis.

The recognition of glandular fever must depend in the first place upon the exclusion of local lesions, such as tonsillitis and pharyngitis, to which the adenitis might be secondary. The history and

circumstances of the case must be taken into consideration. Rubella is believed by some to occur occasionally without rash, but with marked swelling of the glands along the sternomastoid muscle. Further, some evidence exists to show that mumps may occasionally affect the lymphatic glands of the neck, without any discoverable inflammation of the parotid or other salivary glands. If the patient be known to have been exposed to the infection of either of these diseases, it will therefore be prudent to give a guarded opinion.

Treatment.

There is no evidence that either the course or the duration of the attack can be influenced by treatment. The pain and swelling of the neck may be relieved by the use of fomentations, cold compresses, or belladonna applications; but the employment of these local remedies will not prevent the occurrence of adenitis on the opposite side. The constipation is best treated by a dose of castor oil in the early stage, followed by minute doses of calomel (gr. $\frac{1}{12}$ to $\frac{1}{10}$) twice or thrice a day, but Park West gives warning against purgative doses of calomel, which he has observed to be followed by greater depression and prolonged convalescence. When the pain in the abdomen is severe it may be relieved by hot applications to the surface. Diarrhœa occurring at the time of defervescence should not be hastily checked, and in particular it is inadvisable to give opium for this purpose. If it continue during convalescence it should be treated by small doses of castor oil and ipecacuanha in emulsion, guarded if necessary by a minute quantity of opium, which, however, may usually be dispensed with. The abdomen should be covered with a woollen belt or cotton-wool pad, and the extremities should be protected from chill. As soon as possible the child should be got out into the open air and given iron, tonics, and cod-liver oil. The diet should be plain and nourishing, and should consist largely of cereal preparations and plenty of fresh, sound fruit (oranges in particular). Change of air to a bracing locality may be recommended as soon as the enlargement of the glands has disappeared, or at latest after convalescence has been established for two or three weeks.

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WHOOPING-COUGH.

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WHOOPING-COUGH.

Synonyms.—Pertussis (*per*, intensive; *tussis*, cough); chin cough, hooping-cough; tussis convulsiva; Italian, *tosse asenine;* French, *coqueluche;* German, *Keuchhusten, Stickhusten, Kink-, Kinn-, Kindhusten.*

Definition.—An acute infectious disease, occurring chiefly in children, characterized by paroxysms of cough in rapid series, threatening suffocation, terminated by a long-drawn, audible inspiration; and accompanied by more or less nasal, laryngeal, and bronchial catarrh.

History.

The early writers did not apparently distinguish pertussis from bronchitis, influenza, or croup. Thus nothing definite is known of its origin. The Greeks, however, are said by Mason Good to have had knowledge of the disease. In 1578 Baillou, of Paris, described it as an epidemic cough, "qui tussis quinta seu quintana quod certis horis repetit." Although Baillou considered it well known, it was still generally confused with other spasmodic and catarrhal affections. In 1791 Danz published the first monograph on the subject. Cullen described it as a "morbus contagiosus, tussis convulsiva, strangulans, cum inspiratione sonora, iterata, saepe vomitus." At about the same time reports of epidemics made their appearance. Large numbers of deaths were reported, particularly from Denmark, Sweden, and Norway. In Ireland it ranked fifth among the causes of death. According to Wunderlich this first period in the history of pertussis was marked by the infinite number of drugs recommended for its relief.

Etiology.

The exact cause of whooping-cough has always been a matter of much doubt. Though now recognized as of microbic origin, the discovery of a specific organism, as reported by recent observers, has not been sufficiently verified to be generally accepted.

In the early history of the disease it was thought to be an affection of the stomach. Bean regarded whooping-cough as a laryngitis; Broussais, as a bronchitis. Pressure upon the vagus nerve, by swol-

len tracheal or bronchial lymph nodes, was considered by Friedleben as the cause. Mussy held this same view. On physiological grounds Baginsky held it to be an inflammation of the larynx and trachea. He pointed out the fact that the superior laryngeal nerve is proved by experiment to be the nerve of cough; and that irritation of areas supplied by this nerve, as the posterior laryngeal wall just below the vocal cords and the trachea to its bifurcation, produces the most intense cough. Mayer-Huni, von Herff, Oppolzer, Loeschner, and Marcus all took the view that whooping-cough depended upon catarrh of the larynx and bronchi. Other writers, as Copeland and Webster, treated it as a pure neurosis, the result of some functional disturbance of the recurrent laryngeal, phrenic, pneumogastric, or sympathetic nerves, or of the medulla.

It now seems certain that these observers were mistaken. Many things refute the neurosis theory; pertussis originates and spreads by contagion; epidemics are common; a single attack causes almost absolute immunity.

The first hint that pertussis was due to some "contagium animatum," came from Linnæus, the great botanist, nearly two hundred years ago. He thought the cause would be found in the larvæ of insects. That this principle suggested then, and so long overlooked, is correct, is beyond dispute. That it is a zymotic disease, with localization in the respiratory organs, was first proclaimed by Canstatt and Lebert. Gerhardt classifies it, not with pulmonary diseases, but between meningitis and cholera. Fleischner puts it between croup and mumps.

Bacteriology.

A great deal of work has been done, in quest of a specific microorganism. Poulet, Hallier, Letzerich, and Bürger have described varieties of bacteria found in the sputum, but have failed of any proof of pathogenesis. A protozoön found in the sputum by Deichler was considered by him the cause.

Cohn and Neumann reported the results of sputum examination in twenty-four cases of pertussis, in children from one to ten years of age. At the end of a spasm the sputum was placed in a Petri glass, washed thoroughly with distilled water, and a small portion dried and stained with carbolic methylene blue. Diplococci and short chains of small cocci were observed. The authors, however, did not assume that these were necessarily the specific germs of the disease.

A. Moncorvo concluded, from his bacteriological researches, that the microorganisms discovered by Moncorvo, Sr., were true bacilli which could be cultivated in suitable media; and that pertussis could

be transmitted to animals by inoculating them with pure cultures of these bacilli. Ritter, of Berlin, described a very small coccus, found in the sputum, which he believed to be the pathogenic germ of the disease. In nineteen cases he collected the secretion from the mucous membrane of the larynx, at the end of a paroxysm of coughing, placed it in a sterilized vessel, and carefully washed it with distilled water. Small opaque particles were found, and these he cultivated on agar-agar. Small colonies were obtained within twenty-four hours; these were grayish and opaque, and adhered firmly to the surface of the culture medium.

Very promising observations were made by Afanassiev. He isolated from the sputum of pertussis patients a short, thick bacillus, which he cultivated upon beef peptone and agar-agar. In many points this differed from the bacilli that had been previously described. Pure cultures of this, inoculated upon the respiratory mucous membrane of dogs and rabbits, produced symptoms simulating whooping-cough and bronchopneumonia. After the death of the animals this same bacillus was found in the mucous membrane of the nose, trachea, and bronchi. It was also found in the lungs and bronchi of children who had died of the disease. So the author considered it the true cause of whooping-cough, and named it the *bacillus tussis convulsivæ*. Schwenker and Wenat confirmed these observations. Semtchenko, after careful investigation, concluded that the bacillus of Afanassiev is specific; that as early as the fourth day of the disease it may be found in the sputum; that it multiplies in the body, and as it increases, the severity of the disease diminishes; that when the paroxysms are reduced to two or three a day or less, it disappears; that if bronchopneumonia develops as a complication, it increases in the sputum.

Koplik, of New York, has very recently isolated a bacillus that closely resembles the one observed by Afanassiev in film preparations, this latter being, it is believed, not identical with the one which Afanassiev obtained in culture experiments. Koplik found this bacillus, in thirteen of sixteen cases of whooping-cough examined by him, in the expectorated mucus. The expectorated material was received directly in Petri dishes, the mucous aggregations being readily removed after time had allowed the frothy matter to disappear. The bacilli were seen as very minute rods with rounded ends, sometimes having the appearance of diplococci because of a deeper staining at the extremities. The rods varied somewhat in size, but were as a rule very little larger than the influenza bacillus. The best culture media were found to be blood serum and hydrocele fluid, but cultures were obtained in bouillon, agar-agar, and gelatin, though not on

potato. The bacillus is anaërobic and motile. These discoveries of Koplik have since been confirmed by Czapelewski, of Cologne, who, however, thinks that the organism is non-motile. Inoculation experiments failed to produce the disease in animals, but as it is not known whether any of the lower animals are susceptible to whooping-cough, these negative results are not conclusive. Czapelewski, while conducting his investigations, was seized with a severe coryza, attended by more than ordinary constitutional disturbance. Examination of his nasal secretions during this attack revealed the presence in abundance of these same minute bacilli. On one occasion also he had a convulsive cough with a fairly characteristic "whoop."

Griffiths claims to have found a ptomain or toxin in the urine in cases of pertussis, which does not exist in the urine of patients suffering with any other disease, or in that of healthy individuals. He also says that he has found the same toxin in cultures of Afanassiev's bacillus.

The mucous membrane of the larynx and trachea is without doubt the seat of a catarrhal inflammation, and any irritation of this so-called "cough area" will provoke a spasm. For instance, the lodging on this area of a bit of mucus which has been raised from the bronchi or trachea will provoke a convulsive cough. But a cough with the characteristics of whooping-cough cannot be produced by mechanical irritation at any time other than during the course of this specific disease.

Thus it seems fairly certain that pertussis is caused by a specific microorganism, whose toxin has a selective action on the centres of the vagus and superior laryngeal nerves. Without further verification, however, there is still some doubt as to the identity of the specific germ, although the weight of evidence at the present time seems to point in favor of Koplik's bacillus.

Mode of Infection.

As a rule, contact with or fairly close proximity to a patient is necessary to acquire the disease; but the exposure may be very brief. It seems possible to contract the disease in the open air. Rarely is the infection conveyed by a third person, and then only if contact with the patient has been close, the person going to another child without the precaution of changing the clothing.

It is very rare for the disease to be spread merely through the agency of an infected room or clothing, as is common with measles, diphtheria, and particularly scarlet fever. Probably the sputum, possibly the exhaled breath, is the germ-carrying medium.

PREDISPOSITION.

Age is the great predisposing factor. Vladimirov gives the following figures showing the ages of 4,623 pertussis patients treated between 1876 and 1887 at the St. Vladimir Hospital for Children, in Moscow:

Under 6 months	5.5 per cent.	From 6 to 7 years	6.1 per cent.
From 6 to 12 months	11.1 "	" 7 " 8 "	4.7 "
" 1 " 2 years	18.1 "	" 8 " 9 "	4.1 "
" 2 " 3 "	14.2 "	" 9 " 10 "	3.3 "
" 3 " 4 "	11.6 "	" 10 " 11 "	1.7 "
" 4 " 5 "	9.1 "	" 11 " 12 "	1.3 "
" 5 " 6 "	7.9 "	12 years and over	1.3 "

The statistics of Szabo (Budapest), compiled from the records of one clinic for thirty-four years, give the ages of 4,591 patients:

Under 1 year	1,028	3 to 4 years	904
1 to 2 years	1,008	4 " 7 "	803
2 to 3 "	659	Over 7 "	189

Holt puts the percentage of cases of pertussis occurring during the first two years as high as fifty, while from the above figures Szabo makes it forty-three, and Vladimirov but thirty-four.

The limits of the age of susceptibility are extreme. The percentage of cases under six months is small, and nursing children are fortunately less commonly attacked. Many exceptions are, however, reported. Rilliet and Barthez reported a case in which the cough set in on the day following birth, the mother having contracted the disease four weeks before her delivery. A case of a child infected on its second day of life and having a well-marked whoop by the eighth day, was reported by Bouchut. Currier observed a child in whom whooping-cough developed at the age of ten or eleven days. At the time of its birth, the mother had a persistent cough simulating whooping-cough, but without the whoop, while two other children in the family had undoubted pertussis. A child under the observation of Holt was attacked on the twelfth day of life. The mother had pertussis at the time of the child's birth.

The rarity of pertussis during the late years of life is due to the fact that most persons have had an attack during childhood, which practically insures immunity. There is also undoubtedly a much diminished susceptibility. Cases have been reported by Berger occurring in a woman aged fifty-seven, and by Heberden in a woman aged seventy, and in a man aged eighty. In cases at any such age the disease runs a very mild course.

Sex.—Girls apparently are more susceptible than are boys of the same age, in about the ratio of five to four. And for some reason the disease seems to run a more severe course in girls.

Previous health seems to bear upon the susceptibility. Undoubtedly children who have become ill nourished from any cause are more likely to contract the disease. Many observers believe that measles is very apt to be followed by pertussis. Vladimirov, however, from his wide observation concluded that measles was in no way a predisposing cause of whooping-cough.

Season, climate, and geographical position apparently have no influence. By many, epidemics are supposed to be nearly twice as prevalent in the winter and spring as in the summer and autumn. On the other hand, Vladimirov says that all the epidemics in Moscow occurred during the summer months, and recurred at regular intervals of two years (1880, 1882, 1884, 1886).

The disease is more common in the civilized countries, which can probably be accounted for by the fact that it has not yet been introduced or firmly established in the more sparsely peopled countries.

The susceptibility to pertussis is peculiarly great, being second only to that of measles. In an epidemic reported by Biedert, of 401 children exposed, 366, or 91 per cent., contracted the disease.

Infectious Period.

That infection can be conveyed from the very beginning of the catarrhal stage is certain. Just how long the source of contagion exists in a given case, it is impossible to say. The spasmodic stage may be so long drawn out by the acquisition of fresh cold, especially during the winter months, that for fear of spreading the contagion patients are frequently isolated from four to five months.

Pathological Anatomy.

Authorities disagree with regard to the lesions of pertussis. Von Herff, in studying the disease as it occurred in himself, observed a marked congestion of the mucous membrane on the under surface of the epiglottis and on the interarytenoid folds, with small deposits of mucus, especially on the posterior laryngeal wall. He thought that the removal of these bits of mucus aborted the attack. Rehn found the anterior laryngeal wall the portion involved, the posterior being perfectly normal. Rossbach in cases of pertussis found all portions of both the trachea and larynx perfectly normal. Thus it has come to be recognized that uncomplicated whooping-cough has no gross pathology. In sudden death in the midst of the disease from convul-

sions or from prolonged spasm of the glottis without general convulsions, venous engorgement of the viscera is practically all that is found. The bronchial glands are sometimes in a state of hyperplasia. The findings in fatal cases of bronchopneumonia are the same as under other circumstances, with pronounced dilatation of the bronchi proportional to the duration of the disease, and emphysema at the apices.

Symptoms.

Clinically, whooping-cough is conveniently divided into three stages, following the period of incubation: (1) The catarrhal stage; (2) the spasmodic stage, in which the characteristic whoop occurs; (3) the stage of decline, or convalescence. These, however, are not always clearly defined.

Incubation.—The insidious onset of pertussis makes it almost impossible to estimate with any exactness the period of incubation. Unless the disease can be transmitted from the mother to the child *in utero*, which seems highly improbable, the case reported by Barthez and Rilliet, previously mentioned, would definitely prove that the incubation may be as short as one day. The other limit cannot be sharply defined. A child may be considered free from infection if from fourteen to eighteen days have elapsed after exposure and no cough has developed. Thus the period of incubation varies from a few days to two weeks.

The first stage is marked by all the phenomena of an acute catarrh of the air passages, with a moderate elevation of temperature. The symptoms generally present at this period of the disease are a dry irritating cough which increases towards night, hoarseness, sneezing, discharge from the nose and eyes; and some râles, especially of the dry variety, can generally be heard over the larger bronchi. This stage may last only a few days, or in mild cases may persist through the whole course of the disease.

Second Stage.—Any doubt as to the nature of the disease that may previously have existed during the catarrhal stage is quickly removed as soon as the characteristic whoop or kink occurs. The paroxysm which distinguishes pertussis from all other diseases of the respiratory organs consists of a number of short, rapidly recurring spasmodic coughs, which continue until the air in the lungs is exhausted, followed by a prolonged inspiration, during which the peculiar sound called the whoop takes place. This sound is produced by the inrushing air striking the vocal cords while still in a state of spasm, and therefore sufficiently approximated to be thrown into vibration by the contact. Other paroxysms follow in rapid suc-

cession, and as no air whatever enters the lungs except during the whoop, and the amount being then limited by the constricted state of the glottis, the blood becomes highly venous, with consequent stagnation in the systemic circulation. The face becomes cyanosed and swollen, the eyes are injected or bloodshot and protrude perceptibly, and when the paroxysms are prolonged hemorrhages frequently occur, especially from the mouth and nose. In the early stage the attack terminates with retching, in which only mucus is expelled, but later the stomach is emptied. Blood also accumulates in the lungs, owing to their partially collapsed condition, which materially impedes the pulmonary circulation, and this, combined with the general venous stasis, fully explains the small feeble pulse that exists towards the end of a paroxysm in severe cases. In neurotic children convulsions occasionally occur from the carbon dioxide poisoning, and in rare cases terminate fatally.

Great prostration results from the violent exertion and from the acute suffering that spasm of the glottis alone entails. Nutrition is seriously interfered with, not only by the loss of food, but also from the frequent filling of the systemic arteries with venous blood. In delicate children, when the attacks are frequently repeated, progressive emaciation and exhaustion may reach a fatal termination without any of the ordinary complications. In milder cases, when sufficient food can be taken and assimilated between the attacks, even delicate children bear the disease remarkably well. The intestinal catarrh that usually accompanies this stage in severe cases is probably the result of the venous stasis referred to above. A moderate elevation of temperature and moist bronchial râles are usually present during this period of the disease.

Intermediate between the mildest type of the disease in which there is no spasmodic stage, and the severest form just described, there is another grade in which the paroxysmal character is equally well marked, but there is no whoop. There are the same rapidly recurring coughs, with flushing of the face, which terminate in vomiting or the ejection of mucus without the crowing sound. Either there is less spasm of the glottis—which is not apparent during the expiratory efforts—or the vocal cords are more under the control of the respiratory centre and expand normally with the beginning of inspiration, so that no vibration is possible. The laity generally call this form of paroxysm the kink, to distinguish it from that in which the whoop occurs.

Third Stage.—By the end of from four to six weeks or later the paroxysms decline in frequency and severity, and convalescence begins. The whoop usually disappears, but the spasmodic character

of the cough remains to the end, and usually recurs with every fresh cold for several months or even as long as a year after the disappearance of the disease. These grave, protracted, and relapsing cases are the ones that led Musser to believe whooping-cough to be an autoinfectious disease.

Complications.

Respiratory System.

The most frequent and fatal of the complications of pertussis is undoubtedly *bronchopneumonia.* It is particularly apt to occur in very young and rickety children, and is often preceded by atelectasis. The latter condition is the natural result of the rapidly repeated expulsions of air while none is admitted, when the chest walls are soft and yielding, as in young and rickety children. As the air is driven out the chest sinks in under atmospheric pressure, and the succeeding inspiration being impeded by spasm of the glottis, perfect reinflation does not occur. If the paroxysms are frequently repeated, collapse of the lower portion of the lungs takes place and remains, and pneumonia is then only a question of a little time. It runs a tedious course, is often fatal, but in the vast majority of cases ends in complete resolution. Occasionally it passes into the chronic form, with increase of fibrous tissue, contraction of the lung, and dilatation of the bronchial tubes. In older children croupous pneumonia occurs from exposure to cold, but it is seldom fatal even when complicated with empyema.

Bronchial catarrh, which is more prevalent in cold weather, increases the tendency to pulmonary collapse, because of the notoriously inefficient character of the pertussis cough. The quantity of air that escapes with each cough, and the space through which it passes, are too small to permit of any material effect in expelling the tenacious mucus, which therefore accumulates and is drawn downwards by the succeeding long inspiration, where it tends to occlude the smaller bronchi. Practically the only means of unloading the air passages of their secretions in this disease is the act of retching or vomiting that usually terminates a paroxysm, and is therefore within certain limits conservative.

It seems almost paradoxical to speak of *emphysema* complicating a disease the most marked physical feature of which is the tendency to empty the lungs of their residual air, yet it is of frequent occurrence in severe cases. While both respiratory acts are concerned in its production, it is probable that the most injury is done by the recoil of the compressed air during the ineffectual spasmodic expira-

tions with a glottis that remains almost closed. In coughing under most other circumstances the glottis is closed only momentarily in the beginning of the act, then opens widely, allowing the imprisoned air to escape rapidly; while in pertussis the vocal cords remain contracted and almost in contact through the whole course of the paroxysm. The distending force is exerted principally where the lungs are least protected—that is, at the apices, the chest walls at these parts being practically fixed, while the lower portions are supported by the upward movement of the diaphragm and the recession of the more yielding parts of the thorax. As the amount of air in the lungs is reduced below normal, the distention is kept up by the expansion of that which remains, and this is still further enhanced by succeeding obstructed inspirations which increase the vacuum without supplying the air necessary to restore the equilibrium of pressure. Practically the same mechanism is also concerned in the production of the emphysema so frequently found in the upper portion of the lungs in fatal cases of croup, when death results from obstruction in the larynx. In this disease, as in pertussis, both respiratory acts are obstructed and each plays a part in accomplishing the same result—the former rapidly, because the force is continuous; the latter more slowly, because it is intermittent.

In the emphysematous areas the bronchial tubes are subjected to the same stretching process and undoubtedly become dilated independently of the contraction of the lungs that goes hand-in-hand with atelectasis and protracted bronchopneumonia. Severe and extensive interstitial emphysema may occur. Northrup reports an extreme case. The pulmonary emphysema may be so great as to cause rupture of the lung and pneumothorax. Winocourov has reported a case in a child four years of age. Subcutaneous emphysema of the chest wall, neck, and face is rare, but may occur, as in a case reported by Croker and Hodge.

Alimentary Tract.

Ulceration of the *frænum linguæ* is present in almost all severe cases. It is not pathognomonic, but occurs in any severe cough. It is caused by the forcible protrusion of the tongue against the lower incisor teeth. If the cough is mild, the teeth particularly flat and smooth, or the frænum so short that it cannot come in contact with the teeth, the ulceration will not occur.

Stomatitis is very common in the severe cases, even when the mouth is kept as clean as possible. The ulcers are more apt to be on the gums, about the base of the teeth, than elsewhere. The affec-

tion seems due to the irritation from the vomitus, in those severe cases in which emesis is so frequent.

Vomiting in many cases is frequent, terminating every paroxysm. It may become so incessant as to be a matter of much concern. The patients may rapidly become ill nourished and thus less able to withstand any of the possible complications. Some may even go on to marasmus.

Diarrhœa, particularly in summer, is by no means a rare complication. When complicating pertussis it seems to have a peculiar tendency to become chronic. The acute attacks may be so severe as to set up an ileocolitis. *Prolapse of the rectum*, with or without *incontinence of fœces*, has resulted from the repeated violent paroxysms.

Nervous System.

Convulsions are not uncommon at the end of severe and protracted paroxysms, and are generally due to carbonic-acid poisoning, sometimes possibly to overdistention of the cerebral vessels or even to meningeal hemorrhage.

The cause of the *cerebral paralyses* seems open to doubt. Beside those just mentioned, emboli must be considered the possible cause in some cases. Before the Vienna Medical Club, Neurath showed three cases in which whooping-cough was apparently the direct or indirect cause of the paralysis that existed. In the first two cases no heart lesion could be detected. Strümpell thinks the paralysis due to an acute form of encephalitis of the cortical portion of the brain, somewhat analogous to poliomyelitis.

Trörtzy described three cases of pertussis complicated by *mental disturbance*, difficulty in and *loss of speech*, and loss of power going on to *paralysis* of some groups of muscles. He considered these symptoms due to pathological conditions of the brain, brought about by disturbance of the circulation. The first case was in a child of two years, who became suddenly affected during an attack of pertussis, after a paroxysm, with distortion of the eyes, dilatation of the pupils and blindness, contraction of the flexors of the arm, delirium, Cheyne-Stokes respiration, and diminution of the patellar reflex and of the senses of pain and of touch. At another time there was a general eclamptic seizure, lasting an hour and a half, accompanied by Cheyne-Stokes respiration, and followed by twelve hours of stupor. These attacks diminished and in two months the patient had entirely recovered.

The second case was in a boy of three and one-half years, who had great headache and much difficulty in thinking and speaking.

The third patient, a child seven months old, during the third

week of the disease had two eclamptic seizures, and in the sixth week loss of power in the right arm, which became absolutely paralyzed. At the end of three months the paralysis had disappeared.

Hemorrhage.

In pertussis the hemorrhages that occur are not due to the disease itself directly, but to mechanical causes, brought about by the marked increase in venous blood pressure during a severe paroxysm. The most common is that from the bronchi or pharynx, or both. This occurs in a fairly large proportion of the severe cases, the blood being expectorated. To some children this is a cause of considerable alarm. Epistaxis also accompanies many of the severe paroxysms. Conjunctival hemorrhages are of very much less frequent occurrence. Teillais, of Nantes, noted a rare complication of pertussis in a child four years old, namely, *detachment of the retina.* The case was severe, and remarkable for the hemorrhages that occurred over the entire body. Hemorrhage may take place into the cellular tissues about the eyes. In a case observed by Holt there was bleeding from both ears, with each severe paroxysm, for more than a week. The child had previously suffered from scarlatinal otitis with perforation of the drum membrane. Intracranial hemorrhages are fairly rare, and are responsible for paralyses, disturbances of sight and hearing, and other cerebral symptoms that have been mentioned previously. The hemorrhages may be meningeal or cerebral, but rarely the latter. They are usually small. At the New York Foundling Hospital a fatal case of pertussis was observed, in which there were punctate hemorrhages throughout the cerebrum, a few in the cerebellum, but none in the pons.

The Heart.—Silbermann, of Breslau, in a study of lesions of the right heart in pertussis, stated that in many cases during the attack there may be observed a weakened action of the heart, the pulse being increased in frequency to 150 or diminished to 50 to the minute. He also found dilatation of the right heart, and a systolic murmur of the tricuspid valve. The author reported five cases, four of which recovered. One patient died in an attack of cough, and the autopsy showed great dilatation of the right heart, the tricuspid valve being mechanically insufficient on account of the extreme dilatation of the right ventricle. Koplik, in a study of fifty cases, brought out these points some years ago, when he advised the use of digitalis as soon as venous engorgement became noticeable.

Urinary Changes.—The changes that may take place in the circulation, due to the great venous congestion, again come into evidence

as the probable cause of the albuminuria that occurs in a fair proportion of cases. In eighty-six examinations Knight found small quantities of albumin in sixty-six, in some accompanied by a few hyaline casts. Stefano Mircoli, in a certain epidemic, found albuminuria in from ten to twelve per cent. of the cases, and a mortality of five to six per cent. from acute nephritis.

Blumenthal made complete examinations of the urine in a series of cases of pertussis, and without exception the following were the characteristics observed: Pale yellow, very acid; specific gravity, 1.022 to 1.032; soon after standing considerable uric acid was deposited, which on quantitative examination was found to be two or three times the normal amount. No albumin or sugar was found.

These two observers would thus seem to represent the extremes. Albumin is certainly present in small quantities in a fair number of cases, but to find five or six per cent. mortality from acute nephritis is not at all the usual experience. An interesting urinary constituent in pertussis is the toxin isolated by Griffiths, having an action identical with the toxin of the bacillus described by Afanassiev.

Sequelæ.

Of the sequelæ of pertussis, tuberculosis is the most common and the most to be dreaded. As a predisposing cause of tuberculosis pertussis is second only to measles. It is most generally and satisfactorily explained as a latent tuberculosis, originating in the bronchial lymph nodes, and given a fresh start by the run-down condition of the child and the great pulmonary congestion. In an analysis of the cause of death in five hundred cases of pertussis, as assigned in the death certificates in Washington, Johnston found fifteen due to tuberculosis following pertussis. The other sequelæ, as blindness, deafness, paralysis, etc., are directly attributable to the complications and not to the disease itself.

Recurrence and Relapse.

Pertussis has been considered by some observers as an autoinfectious disease, this opinion being based upon the occurrence of grave and protracted cases. Musser held this view. But the return of the paroxysms after the disease has apparently ceased is in all probability a neurosis, as experience has shown that the disease is not infectious at that stage.

The recurrence of pertussis is extremely rare. Le Gendre saw one case himself, besides which he was able to collect but eight cases.

Diagnosis.

The diagnosis of pertussis is very difficult in the early stage, unless the child is known to have been exposed to the disease. Measles is excluded if no eruption appears by the fifth day. The most important point to remember is the fact that the cough not only persists but increases in spite of treatment that controls an ordinary cold, and that auscultation reveals nothing in the chest to account for it. Mild cases that run their course without the spasmodic element can be diagnosticated only by the duration of the cough. Neurotic children often whoop with a slight cold, but the history of previous attacks of the same character settles the diagnosis. Any doubt that might exist during the first attack would be cleared up in a few days by complete recovery.

There is a greater tendency to congestion of the conjunctivæ than in other coughs. The face is more apt to flush, and the paroxysms are usually worse at night. Vomiting at the end of a paroxysm is a most suspicious symptom. But in the mildest cases where there is no history of exposure the diagnosis is extremely difficult if not impossible.

Prognosis.

Age is the most important factor in the prognosis—the younger the child the greater the danger to life. In infants, especially those under one year, pertussis ranks as one of the most fatal of diseases, and this is due principally to bronchopneumonia which is generally preceded by atelectasis.

The mortality of bronchopneumonia, always great in young children, is increased in pertussis, owing to the persistence of the cause. Emphysema, unless very extensive or interstitial, does not materially influence the prognosis. Recovery from it in the vast majority of cases must be complete, because no evidence of its existence can be discovered in after years. Gastroenteritis among the children of the poor is often a grave complication, especially in the summer months. The exact mortality is difficult to determine. J. Lewis Smith stated that four thousand eight hundred and forty deaths from whooping-cough occurred in New York City in fifty years, which is equivalent to one out of every seventy-nine deaths from all causes. Large numbers of statistics show that the mortality is from three to fifteen per cent., and occasionally higher.

Prophylaxis.

Considering the gravity of the disease, the spreading of the infection has never been as carefully guarded against as it should be. The only prophylaxis is isolation, which to be effective must be complete. When possible the patient should be strictly quarantined. It is difficult to say how long this is to be kept up. It should begin when the disease is first suspected, and be continued until the child has been free from paroxysms two or three days. Paroxysms following such a cessation, as has been pointed out before, are probably neuroses. Usually the disease is not communicable after two months from the onset.

Children with pertussis should not be allowed to attend school, and for parents to take them to the public parks and elsewhere where children congregate is inexcusable.

Children who are delicate from any cause, rachitis, malnutrition, or syphilis, or who seem predisposed to tuberculosis should be especially guarded against exposure, for in such cases the disease is likely to prove serious. If a case of pertussis occur in a family where there are any such children or young infants, these should be removed as soon as possible, as should be done also in case of an epidemic in the vicinity.

As whooping-cough is spread almost solely by personal contact, the same care need not be taken in disinfection that is so essential in scarlet fever. The thorough airing of the apartments occupied, and the usual washing of the linen are ordinarily sufficient. But in institutions, and if infants of the most susceptible age are to use the contaminated rooms, the apartments should be fumigated and the linen disinfected.

Treatment.

General Measures.

Mild cases of pertussis run a favorable course without any special medication. The selection of a suitable diet, which should be liquid when the temperature is elevated, attention to the condition of the stomach and bowels, and living as much as possible in the open air in warm weather constitute all the treatment required. In cold weather only those who are in fairly good condition and free from pulmonary complications should be allowed to go out, and then only in the middle of the day when the air is still and dry. Delicate children and those having complications, who cannot be removed to a warm climate, should have the benefit of as much fresh air as possible indoors by

frequent change from one room to another, the unoccupied room being freely ventilated in the interval. In summer a change from the dusty, germ-laden air of cities to the mountains or seaside is nearly always beneficial, especially in the later stages of the disease. When vomiting occurs at frequent intervals, wasting and exhaustion take place rapidly if food is not given soon after each attack. Milk, which is always ready, is an excellent article of diet under these circumstances, but older children may be allowed to take any digestible solid food desired.

Local Treatment.

This may be divided into three classes of procedure: (*a*) Insufflation of powders into the nose or larynx; (*b*) applications of solutions by a spray or brush or by irrigation; (*c*) inhalation of gases and volatile substances.

Very many substances have been used by *insufflation*. In young children applications by this method probably never reach the larynx; therefore in such cases nasal insufflations are preferable. Quinine has been more extensively used for this purpose than any other drug. Letzerich, who was one of the first to exploit it, combined it in powder with bicarbonate of soda and powdered acacia. With this mixture insufflations were made into the nose, and if possible the larynx, three times a day. Leuriaux treated the disease exclusively by nasal insufflations, three or four times a day, of sulphate of quinine and resorcin in powder, the head being held downward and forward, the applications being made immediately after a paroxysm. Resorcin alone in powder has been used in the same way by Gamba, Swiette, and Soula.

Guttmann reported favorable results from the employment of insufflations of sozoiodol sodium. He treated thirty cases, blowing about three grains of the powdered drug into each nostril, once daily. Six children were treated as in-patients; two of these were discharged cured within eight days; in the other four cases the frequency and severity of the attacks were greatly diminished within from four to six days. The other patients were treated in the dispensary and with good effect, but the improvement was not so marked as in those constantly under care and observation.

Boric acid, iodoform, benzoin, salicylic acid, borate of soda, antipyrin, and tannin have also been used in powder.

Local Applications.—In 1849 Watson recommended the use of a weak solution of nitrate of silver as a local application to the larynx. His good results were later verified by others. Cocaine has been fairly largely used, and certainly does good, but is accompanied by

too many risks to make it at all a safe remedy. Resorcin was advised by Carreras as an application to the pharynx and the vestibule of the larynx. Moncorvo has been a great advocate of resorcin, using it in a two-per-cent. solution, applied to the larynx with a brush once daily.

Other drugs of less repute are peroxide of hydrogen, morphine, bromide of potassium, chloride of ammonium, tannic acid, and salicylic acid.

Nasal irrigation has been used. The best for this purpose is a saturated solution of boric acid.

Inhalations are of more value than any other means of local medication. In 1859 Desmartes recommended the inhalation of the air from the purifying rooms of gas-works. The procedure is not now considered of any value. The most useful inhalations are those of carbolic acid, creosote, and cresolin. The best method of using any of them is by vaporizing a saturated solution in a croup kettle. Creosote seems to give the best results. Lerefait reported thirty-four cases with most satisfactory results. It was noticeable that the vomiting, which had been severe, ceased in every case in from one to five days after beginning treatment. With carbolic acid there is the danger of poisoning from too rapid absorption. Resorcin fumigations were used by Leblond and Baudier, who reported that with this treatment cases rarely failed to recover within five weeks. Naphthalin vapor has been employed by Chavernac, who reported brilliant results. The same remedy was used twenty-five years ago under the name of Vichot's troches. Inhalations of bromoform have been suggested by Baratiers, of Jenguy. Labbé and Oudin reported twenty-two cases, treated during 1895, as greatly benefited by ozone inhalations, which they believed diminished the duration, the intensity, and the number of attacks.

Internal Medication.

The number of drugs that have been used for the relief of whooping-cough is so vast that to do much more than mention them would be decidedly unprofitable, and, moreover, the space allotted to the subject will not allow of it. All but a few of them have been discarded as useless or dangerous. Belladonna, quinine, antipyrin, and bromoform seem to be of more value than any of the others.

Belladonna is of undoubted service in reducing the number and severity of the paroxysms, but for this purpose it has to be pushed until the physiological effects are produced. Half a minim of the fluid extract as an initial dose may be given every four hours, increas-

ing slowly to every two hours. Jacobi prizes belladonna above all other drugs in this disease. He finds the best results when the flush appears in twenty to thirty minutes after each dose. If the flush does not appear, the drug is not being given in sufficiently large doses. Atropine can be given for the same purpose, usually beginning with gr. $\frac{1}{100}$. Illingworth believes belladonna of much value where there is a tendency to collapse, as shown by clammy skin, cold extremities, and puffiness of the face. The disagreeable effects of the drug are so marked that it is almost impossible to continue it for any considerable time.

Quinine has been much used, and by many with very good effect. Baron tried it in fifty cases, with good results in all. In a few children benefit was derived at once, especially on the second or third day, and not later than the fifth or sixth day. Three weeks was the average duration in his hands. The dose employed was gr. $\frac{1}{8}$ per month, and gr. $1\frac{1}{2}$ per year of the child's age, three times daily. Fisher had a similar experience with twenty-seven cases. The dosage was the same as used by Baron, no single dose exceeding gr. 7. The great tendency for quinine to upset the stomach makes it unfit for use in infants. In older children it may cause so much vomiting as to impair the nutrition of the child. If such is the case it should of course be discontinued.

Antipyrin is considered by many of the best observers the most valuable drug known for the treatment of pertussis. It was first recommended by Sonnenberger. Children tolerate it in proportionately larger doses than do adults, and in cases without elevated temperature there is no depressing effect unless there is an idiosyncrasy. It should be started with small doses, increasing until a child of two years takes gr. 2 or 3 every three hours. Antipyrin is Holt's first choice of the many drugs used in whooping-cough. Dubusquet-Laborderie, in three hundred cases treated with antipyrin, reported very good results in one hundred and ninety-seven. Soula and Marfan have recommended its use, and Cumston has found it serviceable. H. Rehn tried a mandelate of antipyrin in sixty cases, using gr. $\frac{3}{4}$ to $1\frac{1}{2}$ for children from three to five years of age. In all but two cases the paroxysms diminished in number, the appetite improved, and vomiting ceased. The salt is obtained by treating antipyrin with mandelic acid. Sonnenberger, of Worms, does not believe that the mandelate is as effective as the pure antipyrin, first suggested by him. Koplik and Knight advise the employment of antipyrin and digitalis to protect the patients from the deleterious effects of paroxysms on the heart and circulation. They use the antipyrin in one-grain doses for each year, the maximum dose being five grains; the

digitalis in doses of one minim of the tincture for each year, the maximum dose being four minims.

Bromoform, which has been extensively exploited, was first recommended in 1889 by Stepp. It is a clear, limpid fluid, not specially disagreeable, with a specific gravity of 2.9—double that of chloroform. The chemical formula is $CHBr_3$. The odor is agreeable, and the taste slightly sweet. Stepp tried it in seventy cases of whooping-cough in children between the ages of six months and seven years, with the greatest success. At the end of a few days the paroxysms diminished, and in three weeks the patients were well. The following formula was used:

℞ Bromoform	gr. x.	(0.66	gm.).
Alcohol	ʒ i.	(4.00	").
Syr. simplicis	ʒ ss.	(15.50	").
Aquæ	ʒ iij.	(93.00	").

M. Sig. One teaspoonful every hour.

Duncan reported some cases, and summarized four hundred and seventy-five that had been reported by Stepp, Neumann, Loenthal, and Scheppers, as follows: (1) Bromoform, in doses of three to five minims three or four times daily, is perfectly harmless; (2) the attacks diminish in number and severity; (3) the first paroxysmal vomiting disappears in two or three days; (4) nasal and other forms of hemorrhage soon disappear; (5) it acts beneficially in complications, largely by giving affected organs a chance to rest; (6) it shortens the duration of the attack.

Opposed to this very favorable report of bromoform is that of Nolden, who relates two cases of bromoform poisoning from the administration of the drug for whooping-cough. At times the patients show a marked narcotic effect, without influence on the paroxysms. To avoid this effect, particularly in children under one year of age, Max Stoss has substituted antispasmin (narceine-sodium and sodium salicylate). The action was not found uniform. He gave gr. ¼ in the form of a two-per-cent. solution, three or four times a day, to children under one year of age. Eröss, from an experience of eight hundred and seventy-four cases treated in different ways, came to the conclusion that bromoform surpassed all other remedies for pertussis at the height of the convulsive stage.

Opium, to produce the desired effect, has to be given in such doses and for such a time that the constipation and gastric disturbances resulting are such that it cannot be used to any purpose.

Many less deserving remedies have been advanced—ergot by Dewar; valerianate of zinc by Mantey, who claims for it results

almost specific; chloral in large doses by Haskell; ouabaïne by Gemmell; resorcin by Concetti.

The great number and variety of remedies that have been and are still employed in the treatment of pertussis is the best proof that none of them is curative. The chief use of drugs in this disease is to lessen the frequency and severity of the paroxysms, and thus in proportion to diminish the suffering and danger of complications.

At the New York Foundling Hospital, where the in-patients average six hundred and the out-patients seventeen hundred children, from newborn to four years of age, the treatment of whooping-cough has always been a matter of much concern and some experimentation. As each new remedy has been brought out, it has been given a fair trial; and, after all has been said and done, no drug has proved of much real value. This is due in great measure to the readiness with which children's stomachs are upset by almost any drug that is used in sufficiently large doses to benefit the whooping-cough.

During the year 1897 a treatment has been tried which has not the objections mentioned: first, the remedy employed is not a drug; and second, it is not given by the stomach. This treatment, which consists in the administration of carbonic-acid gas by the rectum, was suggested by Bergeon, who had been using it since 1887. In this country Rose has advocated its use. During 1897, at the New York Foundling Hospital, one hundred and fifty cases of pertussis were treated by this means. Of the total number, one hundred and forty-three showed very marked benefit. The vomiting ceased even in the severest cases by the second or third day; the whoop disappeared; and the number of paroxysms was reduced to two or three daily. The seven remaining cases were apparently not benefited. One of the seven was well along in the disease before this treatment was instituted. The duration of the disease, so far as could be determined, was not influenced. Not the slightest ill effect of the treatment was observed. During the administration of the gas the face flushes decidedly, and this lasts some fifteen minutes after. In some cases a mild diarrhœa was observed, which was apparently due to the irritation of the rectum by the injection tube. This ceased after suspending treatment a few days, and thereafter using the gas less frequently.

The method of administering the gas is very simple. A wide-mouthed jar, holding a pint or more, is supplied with a perforated cork, through which is a glass tube extending about half-way to the bottom. To the outer end of the glass tube is attached a flexible rubber tube about three feet long, which has at the end a detachable hard-rubber nozzle suitable for rectal injections. The bottle is filled about one-third with water. About six drachms of bicarbonate of

soda is dissolved in this, and there is then added about one-half ounce of crystals of tartaric acid. As the tartaric acid dissolves, the CO_2 is liberated at the proper rate for administration. The rectal nozzle is inserted and the administration of the gas continued as long as desired.

For all children the treatment was given three times daily some two or three hours after meals. In infants the treatment lasted five minutes at each séance; in the "runabouts," ten minutes. The treatment has been the most satisfactory ever used in the institution.

Mechanical Treatment.

Naegeli reported that in two children he succeeded more than five hundred times in apparently arresting the spasms of pertussis by pulling the lower jaw downwards and forwards. His experience, however, so far as can be found, has never been confirmed by other observers.

Spasm of the glottis is the sole cause of the acute suffering in uncomplicated whooping-cough, and could this element be removed, the disease would be reduced to the level of an ordinary bronchial catarrh. The fear that children exhibit on the approach of a paroxysm, when they drop their playthings or other occupation and run to the mother or nurse for relief, is not the dread of the cough or the vomiting that follows, but of the torture that results from prolonged spasm of the glottis. In the adult this feeling is intensified by the sense of impending death, which can never be gotten over no matter how often experienced. It is not the last hour that has come, nor the last minute, but almost the last second. The suffering is not due solely to want of air, because it begins the instant the spasm begins and often when the lungs are well supplied with air. On this point one of the present writers (O'Dwyer) can speak from personal experience, having had whooping-cough when over forty years of age, and complete spasm of the glottis from other causes many times.

Spasm of the glottis being not only the sole cause of the acute suffering in pertussis, but of most of the dangers as well, the main object of medication is the relief of this symptom. The cases in which all attempts at relief by drugs fail are only too common. In many of them the continuance of the severe paroxysms is a great menace to life itself.

In *intubation* we have a means of absolutely relieving the spasm of the glottis. With the tube *in situ*, of course the spasm cannot occur.

With the use of metal tubes in croup, a certain small proportion

of cases occurred in which the tube could not be dispensed with after the disease for which it had been used had ceased. This was due to injuries to the larynx, the most common of which was abrasion of the mucous membrane in extracting the tube, which at the end of three to five days always had more or less calcareous deposit on it. These abrasions led to granulation tissue, which would so occlude the larynx that the tube had to be replaced. This element of risk has made it seem hardly justifiable to intubate for the relief of the spasm of the glottis in pertussis. But with the use of the hard-rubber tubes that are now made, this element of injury to the larynx should be very much lessened, as the tubes when extracted are absolutely free from calcareous deposits, and can thus be worn much longer. So now intubation in these grave cases seems an absolutely legitimate procedure.

At the New York Foundling Hospital, during 1897, three children with pertussis contracted laryngeal diphtheria. The stenosis became so marked that intubation was necessary. While the tube was in the larynx, its effect upon the whooping-cough was interesting. There would appear all the signs of a beginning paroxysm, a spasmodic cough of the usual length so far as expiration was concerned, sometimes even causing cyanosis. But then when the inspiratory effort was made, there could be no glottic spasm, the air entered the lung freely through the tube, and the paroxysm terminated abruptly, without the least sign of distress or vomiting. After the removal of the tube the disease went on as before.

Method of Operating.—The nurse or person who holds the child should be seated on a solid chair with a low back, and the patient placed on the lap with the head resting on the left shoulder of the nurse, in order to leave the gag free. The hands can either be held, or, still better, secured by the side by a towel or sheet passed around the body, and left in that position until the tube has been inserted and the string removed. Fastening the hands in front of the chest or the presence of thick garments in the same location renders it more difficult to depress the handle of the introducer sufficiently to carry the tube over the dorsum of the tongue.

The gag is then inserted well back behind or between the teeth in the left angle of the mouth, and opened widely, care being taken not to do it too suddenly or to use too much force. In children who have not at least one bicuspid on the left side, the gag should not be used, as it slips forwards on the gums, and, besides being in the way, is liable to injure the incisor teeth. There is little difficulty in these cases in keeping the mouth sufficiently open with the finger, if carried far enough to the patient's right to be out of range of the front teeth.

An assistant stands behind the patient and holds the head firmly by placing one hand on either side, and at the same time slightly elevates the chin. The person who holds the head, if without any experience, should be requested not to touch the gag, as this, if properly placed, retains its hold by the pressure of the teeth.

The operator stands in front of the patient, holding the introducer lightly between the thumb and fore-finger of the right hand, the thumb resting on the upper surface of the handle just behind the knob that serves to detach the tube, and the index finger in front of the trigger support on the under surface. When the instrument is held in this manner, it is impossible to use force enough to make a false passage, while if firmly grasped in the hand the beginner may unconsciously exert sufficient force to lacerate the tissues.

The index finger of the left hand is carried well down the pharynx or to the beginning of the œsophagus, and then brought forwards in the median line, raising and fixing the epiglottis, while the tube is guided along beside it into the larynx. Allowing the child to compress the finger between the gums for a few seconds, until the jaws relax, before carrying it into the fauces, avoids the necessity of using force. If any difficulty is experienced in locating the epiglottis, it is better to search for the cavity of the larynx, a cul-de-sac into which the tip of the finger readily enters and which cannot be mistaken for anything else. Once in this cavity, the epiglottis must be in front of the finger, and the latter is then raised and pressed towards the patient's right, to leave room for the tube to pass beside it. The distal extremity of the tube should be kept in contact with the finger, and even directing it a little obliquely towards the right side of the larynx is necessary to get inside the left aryepiglottic fold, especially in very young children.

The handle of the introducer is held close to the patient's chest in the beginning of the operation, and rapidly raised as soon as the lower end of the tube has passed behind the epiglottis; otherwise it will slip over the larynx into the œsophagus.

As soon as the cannula is inserted it is detached by pressing forwards the button on the upper surface of the handle with the thumb, while counterpressure is made with the index finger on the trigger beneath. In removing the obturator—the joint in the shank of which is intended to facilitate this part of the operation—the movements required for insertion are reversed. To prevent the tube from being also withdrawn, the finger must be kept in contact with the shoulder, either on the side or posteriorly. The tube should be carried well down in the larynx before being detached. The gag is removed as soon as the tube is in place, but the string is allowed to

remain long enough to be certain that everything is right. In removing the string the finger must be reinserted to hold the tube down, but the gag is rarely necessary, as children old enough to understand readily open the mouth for this purpose.

In withdrawing the tube the child is held in the same position, and the extractor is guided along the side of the finger, which is brought in contact with the head of the cannula and then pressed towards the patient's right, in order to uncover the aperture and allow the instrument to enter in a straight line. No attempt at extraction should be made until the head of the tube is felt.

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CHOLERA INFANTUM.

BY

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NEW YORK.

CHOLERA INFANTUM.

HEALTHY infants have a normal tendency to loose, liquid, or semi-liquid evacuations from the bowels. The cause of this looseness lies partly in the condition of the intestinal tract, and partly in the nature of the normal food, which is breast milk. Peristaltic movements in the healthy child are very active. The young blood-vessels and lymph ducts are very permeable, and the transformation of the surface cells is very rapid. In this way transudation from blood-vessels and the lymph bodies of the intestine is facilitated. The peripheral nerves are very superficial, more so than in the adult, whose mucous membrane and submucous tissue have undergone thickening both by normal development and morbid processes. In the young infant the peripheral ends of the nerves are longer in proportion than in the adult. The anterior horns in the nerve centres are more developed than the posterior ones. Moreover, through the defective development of the inhibitory centres, the reflex irritability of the young, particularly with regard to intestinal influences, is greater. Besides, the retentive action of the sphincter ani is not very powerful; the fæces are not retained in the colon and rectum, which is straight and adjacent to the steep infantile sacrum, and but little time is generally afforded for the reabsorption of the liquid part of the intestinal contents. All this illustrates the facility with which a moderate or even a copious elimination of liquid stools may take place.

Moreover, the frequency of acids, sometimes normal, in the small intestine, gives rise to the formation of alkaline salts with purgative properties. Hoppe-Seyler found free acids in the fæces in dogs and the human adult. Wegschneider met them in nurslings who received nothing but mother's milk. An explanation of this occurrence may be found in the fact that the quantity of food is often too large; but in many instances the amount of digestive fluid is too small, and thus fermentation is caused in place of normal digestion. Moreover, the diastatic effect of the pancreatic juice is limited at a very early age, and undigested material is carried off. In this way, the movements may become quite loose, without the occurrence of extensive or deep anatomical alterations. Superficial changes, how-

ever, may take place; they consist in the hyperæmia of the surface, in rapid transmutation of epithelium, and the formation of mucus.

Most cases, however, of actual diarrhœa originate in excessive peristalsis, which may be either local or general. If it be limited to the small intestine exclusively, the contents retained in the colon may become dry, and the presence of hyperperistalsis in the former may then be doubtful. It may be caused firstly by irritation of local (intestinal) origin, or secondly by irritants furnished either by the nervous system or by the blood.

The first class embraces improper and indigestible foods, or excessive quantities. The abnormal composition of mother's milk is an occasional cause. Mothers who are sick, or convalescing, or subject to strong emotions, those who nurse too often, or suffer from tuberculosis or syphilis or anæmia, or are pregnant or menstruating, do or may secrete an anomalous milk. The colostrum secreted immediately after childbirth may cause diarrhœa; so may milk which contains too much either of fat, or casein, or sugar, or salts. It is mainly the casein, whose coagulation causes more intense disorders in the young, than the causes leading to stercoraceous diarrhœa in the adult. An excess of fat is very irritating by the formation of acid. It is true that it is not the only element of perturbation in the usual food of the young, viz., milk. The milk sugar and albumin, as well as the fat may give rise to the development of acids. In that respect the albuminoids (casein principally) are not very injurious, even milk sugar is but moderately so; but as the oxidizing power is greatly reduced in gastrointestinal disorders, the products of the decomposition of fat are very active. Together with fat acids, carbonic acid and sulphide of hydrogen are formed. Their irritating effect may give rise to hypersecretion only, but frequently leads to catarrh. A similar effect is caused by purgatives, mainly by salts either medicinal or contained in fruit or certain abnormal milks. Parasites act similarly, from lumbricoids to trichomonads or amœbæ. It is true that when present they have not always caused the liquid stools in which they are found—indeed, in a case lately observed of intestinal ulceration of long duration trichomonads were not found for months, until at last they appeared in incredible numbers, thus suggesting that it was the abnormal condition of the intestine and of its contents which facilitated their existence, and not vice versa. But the occasional improvement of diarrhœal diseases after the removal of such parasites allows of but little doubt that they may be the actual cause of the liquid and offensive stools in which they are found.

The intestines may be irritated by changes of innervation, less, it is true, in infants and children than in adults. Experiments on the

pneumogastric, sympathetic, and splanchnic nerves have furnished ample proofs of their influence on intestinal secretion and peristalsis, but it is mainly clinical observation which has established its existence. Trousseau discoursed extensively on nervous diarrhœa. The gastric and intestinal crises of tabes dorsalis are frequent occurrences. Beard quoted both constipation and diarrhœa among the symptoms of neurasthenia; Möbius claims the same for migraine; the action of tobacco is of daily experience. Nor is it out of place to remember the influence of rapid changes of temperature among the most frequent causes of diarrhœa, in all seasons, and for all ages. Thus the prevalence of bacteria and toxins in our etiological reasonings should not be able to dislodge reflex hyperæmia and secretion from their correct places as causes of disease. Like the nasal mucous membranes, the intestinal surface is profoundly and suddenly influenced by colds. Wet feet and exposure of the perspiring skin to a cold or draught will convince the most obstinate and exclusive claimant of bacterial rights of his dependence on other external factors.

Intestinal irritation, with peristalsis and hypersecretion, is often caused by changes in the blood. Pilocarpine, or salines and other purgatives injected under the skin cause diarrhœa. So does uræmia, sometimes without any anatomical alterations of the pale mucous membrane, other times with catarrhal, ulcerous, or croupous changes depending on the action of ammonium carbonate. Extensive burns of the surface of the body exhibit similar results. They are also observed in malarial poisoning. Infections, such as those in lobar pneumonia, influenza, erysipelas, and septicæmia, may cause intense diarrhœa, with or without visible alterations. Even typhoid fever may give rise to extensive transudations without either catarrh or ulcerations of the mucous membranes. That is mainly so in a certain number of young patients, in whom Peyer's plaques are but slightly developed and but slightly changed. Hodenpyl's latest researches prove that even without glandular changes typhoid fever may exhibit all sorts of typhoid symptoms. Asiatic cholera finally, by its toxin which is absorbed and reaches the intestinal glands, results by hypersecretion and failing absorption, in very copious discharges. We shall see that cholera infantum exhibits the same symptoms.

Symptoms.

Cholera infantum may be preceded by symptoms of gastric or intestinal, or gastrointestinal catarrh, but is frequently ushered in without any prodromi. Vomiting and diarrhœa, often diarrhœa without vomiting, with either a moderate or a high elevation of tem-

perature, are the first symptoms. Vomiting follows the ingestion of food or drink immediately, and may be continued without this cause. In the latter case nothing but mucus and a serous fluid, later bile, are brought up; the latter in small quantity, until its secretion and elimination stop altogether. The alvine discharges are copious and numerous, from half a dozen to two dozen a day. They are acrid at first, alkaline afterwards, and watery. They contain no bile but large masses of intestinal epithelia and bacteria. The abdomen is soft. The thirst is intense, the pulse small and frequent, the voice hoarse or gone, the fontanelle depressed, the skin cool and inelastic to such an extent that it can be raised in folds. At this time the temperature of the cavities, if it was high at all, sinks to or below its normal level. The cornea becomes turbid, respiration difficult, and general collapse sets in. The rapid loss of water from the circulation results in anuria and in thickening of the blood, by which are caused cerebral symptoms depending on the slowness of intracranial circulation, or on actual thrombosis. Listlessness with exhaustion, and convulsions when occurring from those sources are called hydroencephaloid. They are complicated with those caused by uræmia, which originates in the absence of renal secretion. The latter does not depend, however, on the copious loss of liquid through intestinal oversecretion alone, but also on actual nephritis, which is recognized by the presence of red blood cells and leucocytes, and of hyaline, epithelial, and granular casts in the small amount of urine either spontaneously evacuated or secured by catheterization. If the patients live long enough, they develop in the lower extremities sclerema which has the tendency to ascend slowly. Chronic cases, or those which turn to a slow recovery, are also apt to cause furunculosis of long duration, with frequent relapses, great suffering, and possibly change into actual septicopyæmia. Pneumonia, pleurisy, peritonitis, and meningitis may follow. They may be the results of thrombosis, or of the original microbic infection which need not, and seldom does, limit itself to the intestinal tract. Altogether the symptoms of the different stages of cholera infantum are explained in two ways, either by the direct intoxication, or by the abstraction of fluids from the organism.

Complications.

One of the most interesting complications or sequelæ of cholera infantum, indeed of all such intestinal disorders as present or furnish toxins, is that with renal derangement or disease. Like the liver, the kidneys—while their tissues are normal—eliminate microbes from the blood (Biedl and Kraus). This process is increased by diuresis,

an observation which is of considerable value for therapeutics. The first functional change is albuminuria. It may be of no account even when it is cyclical, and when it makes its appearance only when the patients are out of bed, and differs greatly in its import from the formation of casts which depend on morbid processes either in the secreting epithelium or in the intercellular substance. Genuine nephritis, either parenchymatous or intercellular, occasionally with shrinking, with hemorrhage, rarely amyloid, and seldom exhibiting dropsy, retinitis, vascular tension or cardiac hypertrophy, is a very frequent result of intestinal toxicity. In a small hospital containing little more than forty beds, I noticed lately at the same time four cases of nephritis evolving out of and accompanying protracted colitis.

Pathological Anatomy.

When the disease has lasted only twenty-four hours there may be few or no changes in the gastrointestinal mucous membrane. When it has lasted longer, the mucous surface is deprived of its epithelium (under the influence of excessive fermentation and secretion brought about by toxins, nerve influence, or ingesta). Between the gastric glands round cells are deposited in large numbers in the mucous membrane of the stomach. The gland cells are swollen, and according to Fischl and Heubner their nuclei are stainable only with great difficulty. The same round-cell proliferation takes place in the lower parts of the intestinal tract; here also the epithelium of the villi is thrown off. The blood-vessels are dilated and filled with blood. Lieberkühn's glands are rarely intact; they exhibit funnel-like dilatations and an increase of cells, which is also manifest in other glands. Peyer's plaques, too, are large and rich in newly formed cells, which are also found between the muscles. Microbes are met with in large numbers and in many varieties. Bacterium lactis aërogenes mostly in the upper part of the bowels, and B. coli commune mostly in the colon, are common. Among them there are streptococci and liquefying bacilli which are inconstant though frequent in all sorts of diarrhœa. So far as bacterium coli commune is concerned, it was discovered by Escherich in 1885. At that time it was considered to be harmless. But in 1889 it was found by Larnette in two cases of perforation peritonitis; its cultures caused experimental peritonitis in animals. Since that time it has been met with in many tissues of the human body, into which it has emigrated during the moribund state or after death; but it appears also to be settled that it may cause inflammation, suppuration, and sepsis in many diseases, such as enteritis, colitis, typhlitis, peritonitis, cystitis,

pyelonephritis, cholecystitis, meningitis, angina, pneumonia, endocarditis, arthritis, salpingitis, endometritis, lymphangitis, panaritium, gas phlegmon, and puerperal fever. Lately a case of peri- and endometritis was published by Uhlenhuth, who claims that in his patient the bacterium coli exhibited three different degrees of virulence.

Like Escherich, Booker found no specific bacteria in diarrhœas, but mixtures of many; proteus vulgaris was mostly found in the colon, also in the stomach, least in the small intestines. When streptococci are extensively met with, they give rise to symptoms resembling an irregular typhoid fever, and depending either on streptococcal infection or on the absorption of a toxin. All of them are or may be the causes of the palpable changes in the intestinal surface; when they are severe and lead to ulceration, microbes may be swept into the circulation. In this way the lungs are known to be infected. Still it should here be emphasized that intestinal ulceration does not always require the presence and action of bacteria to any or to such a degree as in diphtheritic or gangrenous colitis, where they are mostly in evidence.

The contents of the bowels are copious and thin, exactly like those which are observed in children who have died of convulsions during the hot season. In sunstroke both the stomach and the intestines are apt to be found in the same condition. This similarity is very suggestive. It appears to show that cholera infantum, when fatal on the first day, proves so by paralysis exactly as in insolation. At that early time surely cholera infantum is not yet enteritis. This is primary in the other forms of intestinal oversecretions; in cholera infantum it is secondary. The kidneys are large and pale, with fatty degeneration of the parenchyma, and sometimes pus in papillæ and calyces. Bacterial emboli are rare, certainly much rarer than in the lungs. The liver shows the same cloudy swelling of the parenchyma which is met with in the kidneys. Other pathological changes are the intense rigor mortis, and the dark color and defective coagulability of the blood. The meninges and the lower part of the lungs are hyperæmic.

These results were partly found, and partly confirmed by one of the most industrious and careful of modern bacteriologists who at the same time is a clinician, Booker, who spent years of labor on his researches on the bacterial nature or complications of the different forms of intestinal disorders, both light and grave. He published ninety-two bacteriological examinations, in all of which he found the bacterium lactis aërogenes and coli commune; in most of them also streptococci and proteus vulgaris. The number of his autopsies was

thirty-three; the cases ware classed by him as acute and chronic gastroenteritis. In the former the local alterations of the intestine were but few; but the general infection, including that of the lungs in which bacteria were found, and that of the spleen and kidneys which were mostly affected by toxins, was very intense. The latter exhibited many alterations both of an inflammatory and a degenerative nature, which differed with the localization and the destructive influence of the bacteria. When he met with these same results in the living, the prognosis depended on the clinical symptoms, which differed widely in individual cases. This observation of a pathologist who is at the same time a clinician proves again the insufficiency of pathological anatomy when confined to the dead-house, or of bedside observation when not guided by histological and bacteriological research.

The ubiquitous appearance of a great many varieties of microbes which were present in all sorts and grades of intestinal disorders, induced Booker to venture upon a classification which is partly clinical, and partly bacteriological. He distinguishes three forms of diarrhœal diseases: (*First*) The dyspeptic diarrhœa, with no inflammation, with no leucocytes or epithelia in the lumpy acid stools, with plenty of bacteria coli communia, and few specimens of bacterium lactis aërogenes. This is sometimes an independent form, but other times the first stage of (*second*) the streptococcic gastroenteritis. This has the character of a general infection, the intestines are ulcerated or suppurating, the stools contain mucus, leucocytes, and streptococci. These are sometimes very numerous, in some instances mixed with bacteria coli communia. When cocci are prevalent, the cases are very obstinate and fatal. Booker's *third* form is a bacillary gastroenteritis. It exhibits less local inflammation than intense toxæmia. A great many varieties of bacilli are found, with or without streptococci. Not one of these three classes, however, is claimed as a clinical or pathological entity; on the contrary, *transitions* between them are pronounced to be very frequent.'

After all, observers agree in the absence of a constant and pathognomonic microbe. Among others Baginsky and Stadthagen found a body (probably basic) in the cultures of a bacillus from cholera infantum which is probably identical with one obtained by Brieger in decomposing horseflesh, that is very poisonous, acts on frogs like curare, dilates the pupils, and stops the heart in diastole.

Etiology.

The theories established for the explanation of cholera infantum changed with those governing etiology in general. Fifty years ago almost all the diseases of the infant, and some of the mother, were traced back by Thomas Ballard to "fruitless sucking." Infant cholera was by some considered identical with Asiatic cholera. Some unknown atmospheric influence, sewer emanations of undescribed nature, evaporations of the upper strata of the earth, malaria, moisture, the oscillations of the barometer, or of the subsoil water were charged with being the causes of cholera infantum, with equal and positive fervor.

When etiology became more bacteriological, microbes were accused, for instance, those of the genus ascophora by Bouchut; others looked for poisons, as Sonnenberger, for the presence in the food of plant alkaloids.

The temptation to attribute cholera infantum to the direct influence of microbes was combated by the fact that too many of the latter were found, and that it became difficult to identify a single one as the cause of cholera infantum. Neither Escherich nor Baginsky nor Booker convinced himself that there was a direct connection between the presence of special bacteria with the symptoms of cholera infantum. Baginsky found twenty species or varieties of bacteria, mostly saprogenous, none of which could be claimed as pathogenous. Thus chemistry, after having long been neglected, had to be called in. Uffelmann and Seibert accused the decomposed milk sold in large cities, Lesage a poison produced by some microbe not specific, Vaughan his tyrotoxicon. The poisonous substance would, in the opinion of many of these authors, be evolved out of milk, even out of breast milk. Difference of opinion, however, became apparent in regard to the question whether the poison entered ready made with the milk, or was developed out of it in the alimentary tract of the infant. Both of these opinions are founded on facts; in many cases both roads were found accessible to the poison.

The first stages of cholera infantum do not look alike. Some cases begin very abruptly, others have a slight gastrointestinal disturbance or prodrome. The patients are less than two years old. In the vast majority the feeding is artificial, and with but few exceptions the attacks occur during the hot months of the summer, on such days as furnish only a slight difference between the temperatures of day and night, and during the weeks following them.

Constant heat is undoubtedly a prominent etiological factor. It

appears, however, that when and where the babies are habituated to a warm climate, they do not suffer like those who are suddenly exposed to excessive temperatures. The differences of temperature, as collated by Meinert, between January and July, are in Africa 3.4° C. (6.1° F.), in South America 4.2° (7.5° F.), in Australia 13° (23.4° F.), in central Asia and Europe 26.1° (47° F.), and in North America 28.4° C. (51.1° F.). The sudden heats of the temperate zones are among the principal causes of cholera infantum; in them it is most frequent, though it be found in warm climates.

How does heat affect the babies, indirectly or directly? Its indirect effect is best appreciated when it is remembered that breast-fed babies do not suffer like those artificially fed. Meinert's observations in Dresden[5] yielded eighteen deaths among the former, four hundred and sixty among the latter in eleven hot summer weeks. This agrees with what every practitioner learns from his own experience. That coarse and fermentable food leads to catarrhal irritation of the intestine which may precede cholera infantum, or to the formation of a toxin or toxins which cause it without a previous anatomical lesion, is easily understood.

Is there anything like a direct influence of heat on the baby with the result of causing cholera infantum? It has always appeared so to me. In a brief paper read before the Verein Deutscher Aerzte in 1858—it is contained in the minutes of the society—I took that stand; and again in 1868 in a paper[6] entitled "Concerning the Neglected Causes of Infant Mortality in the City of New York." Twenty years ago Clarke Miller[7] pointed out the striking resemblance between cholera infantum and sunstroke. He claimed the symptoms belonging to the former as due to paralysis. Meinert shares his opinion to its full extent.

Both are diseases of the hot season, and caused by uninterrupted heat. Hot days relieved by cool nights are well tolerated; it is the constant heat which proves detrimental. Constancy is still more dangerous than temporary excess. A relatively lower temperature, but relentless and moist, demands most victims. High temperatures with wind and drought are comparatively safe; absence of ventilation is destructive. No wall ventilation takes place during summer; and in the first weeks of the autumn the houses remain warmer than the surrounding air, for the soil retains the temperatures soaked in during the summer. All this is worse in large cities, in crowded streets, where the buildings are high and exclude wind and draught, in narrow flats or tenement houses, in residences with scanty windows looking in one direction only. In them the babies are housed, there they are stifled in their beds. If they be breast fed, they are now

and then taken up and changed about. If not, they are given their bottles in their cribs without perhaps changing their positions. Lehmann experimented on such babies buried in their beds, and found that they inhale four times the amount of carbonic acid received by those not so buried. They are the ones that are liable to suffer, though or rather because they are not exposed to the sun, from isolation; they are the very victims of cholera infantum. For in addition they lack what is most essential to keeping up circulation and tissue metamorphosis, viz., water. Sweltering in their unclean and hot bed prisons they are given the exact food they receive on cool days. The very adults who will satisfy their thirst by copious draughts of water, will never think of giving an extra allowance of it to their starving young ones. The breast-fed infant is better off in that respect also. The mother or nurse, drinking *ad libitum*, dilutes her milk, for breast-milk is no unchangeable article like the Gordon-Walker or Gaertner; it may change in certain limits its percentage of constituents every hour of the day, every day of the week.

The question whether heat causes cholera infantum by its direct or indirect effects is therefore easily answered. It acts in both ways. By fermenting and spoiling the baby's food, mainly cow's milk, it produces deleterious ptomains. By paralyzing its nervous system it causes the characteristic gastric and intestinal disturbances, over-secretion and non-absorption. Both of these need not coincide with, or depend on, catarrhal or other changes of the alimentary tract. But these latter will become apparent when the former have lasted more than a day.

No single cause will always have a uniform effect. Individual power of resistance and vitality increase or lessen the action of external circumstances. A certain predisposition is always required to make a living being submit to a morbific influence. Not everybody suffers from insolation when exposed to protracted heat. Nor is the same food equally dangerous to all. In the foundling hospital of Prague, under Epstein's control, the mortality of the infants is excessive; that of the same class of infants when sent to the country and fed on the same material, is comparatively trifling. In a small ward of a hospital or in a private room of a poorly equipped residence the mortality of infants is not so great as in large wards or big institutions. When thirty years ago I proved that in such a one every infant that was kept a few short months died, I was expelled for my pains. Still the fact remains exactly so. One of the most assiduous and learned pediatrists of modern times, Heubner, had the same experience. He expects the little waifs in his hospital to live only when he is able to transfer them to the country, or to their own poverty-

stricken homes. Thus not even better hereditary influence, or constitution, or previous good condition are safeguards; and bad food alone is not the only detriment.

It should not be forgotten that in many cases the fatal intestinal disorder is of microbic origin, or is readily becoming complicated with microbes and their toxins. They are contagious. There is no hospital or nursery ward without them. The clothing and bedding are soiled, the nurses stain their fingers with it, and going from one baby to the other, feeding, washing, changing clothes, infect one after the other from a single source. Infection of the intestinal tract takes place not only through the mouth but also through the anus. This source of infection is almost unavoidable. Heubner succeeded in reducing his mortality by more than twenty per cent. by simply employing a set of nurses for the exclusive duty of attending to the diapers, and another set for feeding and other attendance. As long as a single nurse has the whole attendance on a number of infants, absolute cleanliness of her fingers is practically an impossibility. If in every such institution the mother could be kept with her infant, the danger of contagion would be relatively small.

Diagnosis.

The diagnosis of "cholera infantum" becomes difficult only in those cases which have developed out of catarrhal conditions of the alimentary tract under the same influences which give rise to all sorts of disturbances, viz., constant solar heat and inappropriate feeding. For the purposes of practice an exact diagnosis in difficult cases is perhaps not always very important. For no matter what the case may be called, the indications presented by the local changes in the alimentary tract and by the constitutional symptoms exhibited by the patients are more or less identical. Still the diagnosis of "cholera infantum" from other forms of gastrointestinal disturbances should be made; in many of the latter the successful treatment depends on the exact knowledge of the condition of the bowels. There are several forms of diarrhœa which should be known in this connection, viz., fat diarrhœa, catarrhal enteritis, and follicular enteritis.

The name of "*fat diarrhœa*" was given by Biedert to a condition in which the normal proportion of fat in the infant fæces, which amounts to from four to twenty-five, mostly from nine to eleven per cent., is increased to from forty-one to sixty-seven per cent. In this form of diarrhœa the discharges are shining and glossy with fat, of yellowish or gray color, sometimes greenish, mixed with mucus, and mostly very malodorous. The fat molecules are large, in the normal

fæces small. It should be remembered, however, that the percentage of fæcal fat is liable to be increased in every attack of dyspepsia (Tschernow, Uffelmann).

This fat diarrhœa may be primary or secondary. The first is the direct result of the ingestion of an excess of fat, and is relieved by correcting the composition of the food. Fat should be diminished, and sometimes withheld altogether. For some days the substitution of egg water (albumen beaten up in water or in barley or toast water), or of a thin chicken broth is advisable. There are some babies who from the moment of birth bear milk, even breast milk, in great dilution only—an illustration of the justice of my demand of ample dilution of the food given to the newly born and very young.

The secondary form of fat diarrhœa, not depending solely on an excess of fat, is due to catarrhal conditions of the intestine, or to disease of the pancreas. In autopsies duodenal catarrh, a large size and dry condition of the pancreas, a contraction of the orifice of the choledochus and pancreatic ducts, parenchymatous pancreatitis and fatty degeneration of the liver have been found. A moderate amount of the latter, however, is met with under normal conditions of the baby.

In *intestinal catarrh* (catarrhal enteritis) there are fever, diarrhœa, and pain, and when the affection begins in the stomach, vomiting also. The babes are pale, and draw up their legs, and when the catarrh descends to, or begins in, the rectum, there is tenesmus. The evacuations in the beginning contain remnants of food, and have a stronger odor than normal fæces, still they are not very offensive; afterwards they are liquid, light yellowish or brownish in color, strongly acid, but later of an alkaline reaction, with many specimens of bacteria (none of which is characteristic of the affection), epithelium, mucus, sometimes pus, and remnants of food of all kinds; the percentage of water is very large, amounting to ninety to ninety-five per cent., while in normal fæces of the nursling it is but eighty-five per cent., and in older children eighty to seventy-five per cent.; particularly is the percentage of water large in all those cases of diarrhœa which depend upon, or are complicated with, disturbances of the circulation brought on by diseases of the heart, the lungs, or the liver. If the evacuations were first odorless, they become fæcal, afterwards acid, and in protracted cases and so-called follicular enteritis, cadaveric.

In the beginning of the disease there is sometimes herpes labialis, and the urine is diminished in quantity, but is entirely arrested only in the very worst cases which have a tendency to become choleraic. In a few cases recovery is quite rapid; in others the disease terminates in so-called follicular enteritis, or in chronic intestinal catarrh.

When there is diarrhœa we have to conclude that the upper part at least of the colon is affected. Food remnants will require two or three hours to pass from the pylorus to the cæcum; until then the contents are fluid. Below that point they become rather dry; not so when part of the colon is also in a catarrhal condition. Thus, when they are quite fluid, an affection of the upper part of the colon necessarily exists and results in undue peristalsis.

Duodenal catarrh can be diagnosed only when it is complicated with jaundice, as, when uncomplicated, it never gives rise to diarrhœa. Catarrh of the jejunum and ileum is seldom isolated without the upper part of the colon participating in the process, and it must be supposed that they are disordered when the stomach is affected in a case of diarrhœa. When the fæces are fairly solid and contain conglomerate masses of mucus thoroughly mixed with the fæcal masses, we make the diagnosis of isolated catarrh of the small intestine. Further, when the fæces contain a great deal of undigested material we may also conclude that we have to deal with a complicated catarrh, involving both the small intestine and stomach; this is the condition in which undigested food is seen in the fæces (*"lientery"*). But it must be remembered that gastric catarrh alone, with anæmia and abnormal peristalsis of the stomach and upper part of the small intestine, is of itself able to propel undigested food with abnormal rapidity.

When there is bile in passages of green color, yielding a distinct reaction with nitric acid, and attached to the mucus and cylindrical epithelium and round cells, we have also to conclude that the catarrh has its seat in the small intestine, as under normal conditions there is but very little or no bile in the large intestine.

It has been stated that when there is considerable peristalsis and rumbling (audible or perceptible on palpation) in the middle of the abdomen and its lower part, the affection is in the small intestine; that they are lateral and in the upper part, when the large intestine is involved. Still, neither pain nor locality is absolutely pathognomonic. There is one condition, however, that is so. When the mucus is not thoroughly mixed with the fæces, when the fæces are wrapped up in or covered by it after evacuation, then the mucus comes from the colon, and we have to deal with a catarrh of this part of the intestine; and when the fæces are still solid, the catarrh has its location in the lower part of the colon.

As a general rule, acute catarrh of the lower part of the colon generally furnishes pure mucus mixed with blood, particularly in the catarrhal form of dysentery. When the secretion from the colon is very considerable, the bowels are evacuated more or less frequently, in large quantities or smaller ones, suddenly and with a gush, and

usually without tenesmus, which is observed only when the lower portion of the rectum is involved in the morbid process.

In *follicular enteritis* the pathological changes are those of catarrh, but the most severe alterations take place in the solitary follicles and in Peyer's patches. Both of these are enlarged and prominent, and grayish or grayish-red, the latter surrounded by a red zone; now and then ulcerations are found. The microscope also reveals a large number of newly formed round cells, disintegrated or not. In the ulcerations there are large masses of detritus and bacteria. The lymph vessels and lymph bodies participate in every severe form of intestinal catarrh, and there is a large amount of acute and chronic tumefaction of the mesenteric glands.

The symptoms vary according to whether this particular form is connected with acute or chronic intestinal catarrh. In the first variety there are fever and diarrhœa, frequent and copious discharges, all accompanied by pain; the inclination to evacuate the bowels is constant, and there is some tenesmus. When the latter is present, the passages are small, greenish, foamy, have an insipid, musty, and after a while, cadaveric odor, are covered with mucus, some blood and pus; actual hemorrhage is rare. Under the microscope are seen mucus, blood, pus, and round cells, unchanged or undergoing disintegration, and bacilli and zoöglœa.

The symptoms are liable to increase very rapidly, and complications with pulmonary diseases and peritonitis are not infrequent. Although the disease is a very serious one, slow recovery may take place.

Prophylaxis.

There are many measures of a public character that would, and could, be taken in the interest of prevention of cholera infantum and all other intestinal diseases in a more advanced condition of public hygiene. The demand for more air space to the individual, for the separation of, and less stories in, tenement houses, for protection against the sun in our streets, for extensive street sprinkling, for street cleaning, for an abundance of large and small parks and covered piers, for public baths reserved for infants and children, for a close and strict supervision of our markets by the health departments, will be complied with in some distant future when human society and the state recognize their responsibilities to the individual in contradistinction to the egotism and individualism of the present. Indeed many questions of the public hygiene and welfare are of a social and politico-economic nature only; and the safety of the individual depends on the sense of responsibility demonstrated by the

state through its laws and institutions established and managed in the interest of all.

Private houses and rooms should be kept cool in summer and well ventilated. Our windows, which can never be opened more than half, are badly arranged. If a prize had been set on faulty construction it would have been awarded to the man who devised our present arrangements for light and air. The dwellings in the tenements of the poor, with windows on one side only, with an impossibility of procuring a draught, are the main sufferers from these windows of which the upper half only can be lowered or the lower half raised.

No weaning should ever take place in summer, except for very urgent reasons, and with the possibility of procuring good substitutes, inclusive of fresh or aseptic milk. To this the most careful attention should be given. No family should be without red and blue litmus paper, to make sure of the absence of acidity. Altogether the rules which have been published by the Health Department of this city these thirty years, with but slight modifications of and additions to my original draft of 1866, have proved useful and successful.* Diarrhœas must not be neglected. Diarrhœa from "teething," if it

* The original draft of those rules, which was but slightly altered afterwards, was as follows:

If *you nurse your baby:*

Do not nurse your baby oftener than once every two or three hours.

Do not nurse a baby of more than six months oftener than five times in twenty-four hours. When it is thirsty in the mean time, give it cold water. In very hot weather only, mix a teaspoonful of whiskey with a tumblerful of water.

If *you cannot nurse your baby:*

You cannot bring it up without milk. But the milk (cow's milk) must not be given pure, nor with water.

Boil a teaspoonful of barley, ground in the coffee-mill, with a gill of water and a little salt for fifteen minutes, then add half as much boiled milk and a lump of loaf sugar, and give it lukewarm from a nursing-bottle.

Bottle and mouthpiece are always to be kept in water when not in use.

Babies of five or six months, half barley water and half boiled milk, with salt and loaf sugar.

When the bowels are costive, take farina instead of barley flour.

When they are very costive, take oatmeal gruel; strain it before mixing with milk.

When you have but half enough breast-milk use the same food. Give the food and breast milk alternately so that your milk has time to get fit for your baby to take.

You may give beef tea or beef soup mixed with your barley or farina or gruel to babies of five months and older. When ten or twelve months old, a piece of rare beefsteak every day to suck on.

No child under two years ought to eat from your table.

Summer complaint:

When babies throw off and purge, give nothing to eat and nothing to drink for

existed at all, should not be overlooked any more than that depending on its usual causes.

Normal Feeding.

The most important preventive of cholera infantum (as of other intestinal diseases or disorders) is appropriate and digestible food; in the vast majority of cases this is, for the poor infant, human milk. Whenever that cannot be had, proper substitutes should be provided. Among them the milk of the goat and that of the cow take the highest rank. The former, however, contains too much casein and fat, besides being otherwise incongruous. From many of my writings, and mainly from the second edition of my "Therapeutics of Infancy and Childhood" [8] I here condense the following points:

The mixed milk of a dairy is preferable to that of one cow. Cow's milk should be boiled before being used. Condensed milk is not a uniform article, and its use is precarious for that and other reasons. Skimmed milk obtained in the usual way, by allowing the cream to rise in the course of time, is mostly objectionable because such milk is often acidulated. The caseins of cow's and woman's milk differ both chemically and physiologically. The former is less digestible. There ought to be no more than one per cent. of casein in every infant food. Dilution with water alone may appear to be harmless in many instances, for some children thrive on it. More, however, appear only to do so; for increasing weight and obesity are not synonymous with health and strength. A better way to dilute cow's milk, and at the same time to render its casein less liable to coagulate in large lumps, is the addition of decoctions of cereals. Their mechanical effect, however, is not the only one which is obtained. They add to the nutritiousness of the food by their albuminoids, and are certainly not injurious because of their relatively small percentage of starch, for from the very first month of life a distinct diastatic effect is produced by the oral secretion; it increases with every month. Even infusions of the parotids, prepared at different times after death, produce the same effect. Infusions, however, of the pancreas taken from the bodies of infants who have lived three weeks produce no such changes. The diastatic power of the pancreas begins with the fourth week only, and remains feeble up to the end of the first

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at least four or six hours. After that you give a few drops of whiskey in a teaspoonful of ice water now and then, but *no more* until you have seen the doctor.

Stop giving milk at once.

Give no laudanum, no paregoric, no soothing syrups, no teas.

When you see the doctor, trust in him and not in the women. They do not know better than you do yourself.

year. Krüger (1891) found in the fœtus of seven months a sugar-forming ferment which increases towards the normal end of intra-uterine life, is still small in quantity at birth, but then grows so rapidly that it is as active about the eleventh month of life as it is in the adult.

Zweifel experimented with infusions of different glands. That of the submaxillary glands of an infant did not transform starch into sugar, even after the lapse of a whole hour. The effect of an infusion of the parotid of a baby seven days old was distinct after four minutes; however, that of the parotid of a baby who had died at the age of eighteen days, of gastroenteritis, did not act until the lapse of three-quarters of an hour. Nor was a diastatic result obtained by a similar infusion made of the parotids of a baby prematurely born, and of one who died of diarrhœa and debility.

In the healthy baby, however, that diastatic effect is not absent. In connection with this fact it is also important to know that the effect produced by saliva persists in the stomach for a period of from one-half to two hours. But this ceases, and starch will no longer be changed into grape-sugar inside the stomach, as soon as the secretion of hydrochloric acid has begun in the digestive process. This is a very important fact, because it shows that the farinaceous food of the infant or child, though it be not masticated and pass the mouth very rapidly, is in the stomach still under the influence of the saliva. For hydrochloric acid is not secreted at once. The first acids in the stomach while digestion is going on are organic, mostly lactic. This is found to be contained in that organ when gastric juice is removed from it in the first period of digestion. Thus in a gastrostomized boy Uffelmann found under normal circumstances, during the first half-hour, lactic acid only; afterwards hydrochloric acid. The latter is not met with during fevers of any kind, provided the temperature is high, nor during a severe gastric catarrh (nor in dilatation of the stomach resulting from congenital or other constriction of the pylorus). In these conditions farinacea (amylacea) are taken to advantage, principally because the diastatic effect of saliva is not disturbed.

In anæmia and in convalescence, particularly from fevers, the functions of the stomach are impaired. In them both pepsin and hydrochloric acid are wanting. To increase their secretion large quantities of *water* are required.

Infants' food ought to be mixed with large quantities of water, not for the sick only, but under ordinary circumstances. In diseased conditions of the stomach the free dilution of children's nourishment with water is demanded upon the following additional facts. Only to a certain limit, if at all, will pepsin be furnished for digestive pur-

poses. Probably a portion of this is not entirely utilized, because a great quantity of water is necessary to assist in pepsin digestion. In artificial digestion albumin often remains unchanged until large quantities of acidulated water are supplied. Without doubt many disturbances of digestion are to be explained by a deficiency of water, certainly many more than are due to an excess of it, for the latter is speedily relieved by rapid absorption.

When metamorphosis is generally slow, water in abundance increases the elimination of urea and carbonic acid. When the urine is scanty and of too high specific gravity, water protects the kidneys from undue irritation. It acts on the mucous membranes as it does on the external integuments. In laryngitis and bronchitis it liquefies viscid expectoration; in many forms of constipation it acts beneficially by increasing the secretion of the muciparous glands of the intestines. Ice and ice-water, or iced carbonated water, in small quantities, but frequent doses, relieve hyperæsthesia of the stomach and stop vomiting. Another regular addition to the milk food of infants and children should be that of *sugar*. Its percentage in the milk of the woman is larger than in that of the cow. Immediately after the milking of the cow the milk-sugar begins to be changed into lactic acid. This process, after the rennet of the stomach has exerted its coagulating effect, together with the gradual conversion of fat into acid, is the final cause of curdling. The large amount of sugar in woman's milk, together with its smaller percentage of casein (about one per cent.) and butter, gives it the peculiar bluish color and gives to the colostrum of the first days after birth (it contains plenty of salts besides), its tendency to loosen the bowels. This property becomes manifest sometimes under abnormal circumstances. Thus in the milk of anæmic women sugar is occasionally found to an unusual degree. In their cases the other solid matters may also be diminished, still this is not uniformly so. The infants, however, suffer often from obstinate diarrhœa.

The conversion of milk-sugar into lactic acid takes place very rapidly. Under its influence cow's milk turns sour at once. Not infrequently is it acid from the first; it has been found to be so in the udder; in most cases it is "amphoteric," neutral. Thus the question arises what kind of sugar is to be used as the addition to the food of children both well and sick.

Cane-sugar is not so easily transformed. Indeed, it is utilized for the purpose of counteracting the rapid conversion of milk-sugar, and for the preservation of articles of food in general. Trade is not so slow in availing itself of the results of organic chemistry as the medical profession. Condensed milk remains unchanged a long time,

on account of the plentiful addition of cane-sugar, in spite of the original presence of milk-sugar in it. Therefore it is not at all an indifferent matter whether milk-sugar or cane-sugar be added to the food of infants and children. I have always insisted upon the selection of the latter for that purpose. Biedert employs cane-sugar in his cream mixture.

In the sick the absorption of sugar is slower than in the healthy. Besides, during most diseases, particularly those of the alimentary canal, there is more abnormal ferment in the mouth and stomach. Thus but little sugar ought to be given, and never in a concentrated form. Grape-sugar and dextrin are absorbed equally. Cane-sugar, according to Pavy, is partly inverted into grape-sugar and partly absorbed. All appear to be changed, when given in moderate quantities, into carbonic acid and water, even during slight fever.

In that form of constipation of small infants which depends on a relative absence of sugar and superabundance of casein in the breast-milk, the addition of sugar acts very favorably. A piece of loaf sugar (a teaspoonful or less) dissolved in tepid water (or oatmeal water) should be given before each nursing, and will often prove the only remedy required for the regulation of the bowels.

The physiological effect of *chloride of sodium* is very important, no matter whether it is directly introduced through the mother's milk, or added as a condiment to cow's milk, or to vegetable food. Both of the latter contain more potassium than sodium, and neither ought ever to be given, to the well or sick, without the addition of table salt. A portion of that which is introduced may be absorbed in solution; another part is, however, broken up into another sodium salt and hydrochloric acid. Thus it serves directly as an excitant to the secretion of the glands and facilitates digestion. Therefore during diseases in which the secretion of gastric juice is interfered with, or in the beginning of convalescence, when both the secreting faculties and the muscular power of the stomach are wanting, and the necessity of resorting to nitrogenous food is apparent, an ample supply of salt ought to be furnished. The excess of acid which may get into the intestinal canal unites with the sodium of the bile in the duodenum, and assists in producing a second combination of chloride of sodium, which again is dissolved in the intestines and absorbed. Its action in the circulation is well understood; it enhances the vital processes, mainly by accelerating tissue changes through the elimination of more urea and carbonic acid.

A very important fact is also this: that the addition of chloride of sodium prevents the too solid coagulation of milk by either rennet or gastric juice. Thus cow's milk ought never to be given without

table salt, and the latter ought to be added to woman's milk when it behaves like cow's milk in regard to solid curdling and consequent indigestibility.

Habitual constipation of children is also influenced beneficially, for two reasons: not only is the food made more digestible, but the secretions of the alimentary canal, both serous and glandular, are made more effective by the presence of sodium chloride.

A certain amount of *fat* is digested even in fevers of moderate severity, thus also in typhoid fever. But it is a good rule rather to reduce its quantity, because when infants were fed on cow's milk during capillary bronchitis, the fat in the fæces was known to amount to forty per cent. of the solid constituents. A few additional remarks will render the subject clearer, and show that it is very easy to give too much fat.

Infant fæces are comparatively copious, although the baby receives absolutely nothing but mother's milk. What has been called detritus in the fæces is not exclusively undigested casein, but principally fat and large masses of intestinal epithelium. This so-called detritus is not soluble in water, acids, or alkalies, but quite soluble in alcohol and ether. Casein is also present when it has been taken in too large a quantity, or when there is too much free acid in the stomach. In those cases there are large quantities of it in the fæces.

An important practical application of this fact is the following: As it is true that fat is not completely absorbed, even under the most normal circumstances; as free fat acids are so easily formed and accumulated; as they are found in moderate quantities, even in healthy babies; as a surplus is very apt to derange digestion and assimilation, and to prevent the normal secretion of either of the digestive fluids; as there is a superabundance of fat in the normal food of the nursling, the conclusion is justified that we should be very careful in preparing foods for the healthy or sick. It is very easy to give too much fat. It is hardly probable that there is too little. The subject of "fat diarrhœa," which depends on the excess of fat in infant food, has been discussed above (p. 249). It is also well illustrated by the observations of V. and I. S. Adriance.* They have succeeded in proving, by exact chemical and clinical researches, some facts which were known, but perhaps not sufficiently appreciated. Both excessive fats and proteids in the milk of the mother may cause gastrointestinal symptoms in the nursing infant; the former may be reduced by diminishing the nitrogenous elements in the mother's diet; the latter by the proper amount of exercise. Excessive proteids are especially apt to cause gastrointestinal symptoms during the colostrum period, and particularly during that of premature confinement, when their per-

centage is higher. Premature infants are, therefore, in particularly great danger, and their food ought to be greatly modified and watered.

In connection with this question I may also be permitted to allude to the indiscriminate administration of cream and the routine treatment with cod-liver oil in case of sickness; even normal digestion disposes only of a limited quantity of fat (cream, butter, cod-liver oil); twenty-five per cent. of it in the food, as lately recommended,[10] is excessive. One of the preparatory stages of its assimilation is the formation of oleic acid; lipanin, which has been recommended in place of cod-liver oil, contains six per cent. of that acid, the physiological preparation of which the body is spared by its administration. There may be very few conditions in which the digestion is so slow as not to insure some of the required transformation, but in chronic dyspepsia of different sorts fat is badly digested and absorbed, and lipanin may take its place. A small amount of starch is digested at the very earliest age. But cereals containing a small percentage of it only are to be preferred. Barley and oatmeal have an almost equal chemical composition; but the latter has a greater tendency to loosen the bowels. Thus, where there is a tendency to diarrhœa, barley ought to be preferred; in cases of constipation, oatmeal. The whole barley corn, ground for the purpose, should be used for small children, not only the centre (which is preferred because of its white color), because of the protein being mostly contained just inside and near the husk. The newly born ought to have its boiled milk (sugared and salted) mixed with four or five times its quantity of barley water, the baby of six months may take them in equal parts. Gum arabic and gelatin may also be utilized in a similar manner. They are not only diluents, but also, under the influence of hydrochloric acid, nutrients. Thus, in acute and debilitating diseases which furnish no or little hydrochloric acid in the gastric secretion, a small quantity of the latter, well diluted, should be provided for.

This, my method of infant feeding, which is suited for the stomachs and purses of the rich and poor alike, is, however, not the only one proposed and found satisfactory. No single method, indeed, is the only one, nor does it suit every case. It is only an occasional chemist who expects the organic stomach to behave like a chemical reagent; clinicians, however, admit exceptions to the working of their rules and regulations, though their conception were ever so correct and physiological. Still the endeavors to improve the diet of the young, and thereby to remove the dangers of intestinal disorders and the sources of excessive mortality and invalidism, are going on. Nothing has been more successful in that direction than the widespread practice of sterilization and pasteurization of cow's milk. Both are the logical

development of the plan of treating milk by boiling which I have persistently advised these forty years at least, and detailed in my "Infant Diet" [11] in Gerhardt's "Handbuch," [12] in Buck's "Hygiene," [13] in "Intestinal Diseases of Infancy and Childhood," [14] and in my clinical lectures delivered during more than one-third of a century. There can hardly be a doubt that if raw milk could always be had unadulterated, fresh, and untainted, and as often as it were wanted, it would require no boiling. It would even contraindicate it, for high temperatures destroy not only some of the dangerous bacteria, but also those whose action is desirable for normal digestion. Besides, there are those who strongly believe that boiling causes chemical changes. But such ideal milk cannot be had so long as cows are tuberculous, as scarlet fever and diphtheria are met with in the houses and about the clothing and on the hands of dairy men and women, and as typhoid stools are mixed with the water which is used for washing utensils.

Now, what is it that boiling can and will do? Besides expelling air, it destroys the germs of typhoid fever, Asiatic cholera, diphtheria, and tuberculosis, also the oidium lactis, which is the cause of the change of milk-sugar into lactic acid and of the rapid acidulation of milk with its bad effects on the secretion of the intestinal tract. Some varieties of proteus and most of bacterium coli are also rendered innocuous by boiling. Thus it prevents many cases of infant diarrhœa and vomiting, but not all of them, for the most dangerous bacteria are influenced neither by plain boiling nor by the common methods of sterilization. Boiling, or sterilization, is not, however, a safe protection under all circumstances. Aërobic bacteria, the so-called hay or potato bacilli, have very resistant spores, which develop in time. They are found in cow-dung and in the dust of stables, of the soil and streets, and of hay; they render the milk alkaline and bitter; they peptonize casein and liquefy it and make the milk still more bitter. They are very poisonous; their pure culture gives young dogs a fatal diarrhœa. It takes hours of sterilization to kill them; in some instances it required five or six hours. Even the bacillus butyricus takes an hour and a half. But such a protracted sterilization, besides being far from certain in its effect, is a clumsy procedure and one not calculated to benefit the milk. That is why hay-feeding is an absolute necessity, for the bacilli are destroyed by a six weeks' drying. Besides, it is important to keep the stables scrupulously clean, to avoid dirt and dust, to employ peat instead of straw for bedding, to wash the udder and tie the tails before milking, to throw away the first milk, and to remove foreign material from the milk by the centrifugal machine. But no absolute security can be guaranteed. Therefore Flügge adds to his exposi-

tions a warning against some wholesale manufacturers who, always anxious about somebody's—their own—welfare, were (are?) known to conceal the changed condition of the milk and the separation of butter particles by coloring the glass of their bottles.

Whatever I have here brought forward is certainly not to disparage the boiling of the milk; it is meant to prove the danger of relying on a single preventive when the causes of intestinal disorders are so many. It is true, however, that the large majority of the latter depend on causes which may be met by sterilization, but not by sterilization only; also by pasteurization,—that is, heating the milk to 70° C. (165° F.), and keeping it at that temperature for thirty minutes—a procedure which destroys the same germs that are killed by a more elevated temperature without much change in the flavor and taste of the milk. Pasteurization, however, is rejected by H. Koplik.

One of the questions connected with the employment of sterilized or pasteurized milk is whether the milk to be used for a child ought to be prepared at home, or whether the supply may be procured from an establishment where large quantities of milk believed to become immutable for an indefinite period by sterilization are kept for sale. In regard to this problem, Flügge plaintively expresses his regrets that "we have allowed ourselves to be guided by people who are neither hygienists nor physicians, but chemists, farmers, or apothecaries, and whose actions have been based on three false beliefs. Of these the first is that boiling for three-quarters of an hour destroys germs; the second, that whatever bacteria remain undestroyed are innocuous; and the third, that proliferating bacteria can always be recognized by symptoms of decomposition." Nothing is more erroneous. Soxhlet himself, the German originator of sterilization, knew at an early period that the fermenting process is now and then but partially interrupted by boiling, that butyric acid may be found in place of lactic acid, that a strong evolution of gas may be caused after such boiling, and that such milk may give rise to flatulency. Indeed, milk which happens to contain the resistant spores of bacteria becomes a better breeding-ground for them by the very elimination of lactic acid, and the longer such sterilized milk is preserved and offered for sale the worse is its condition. It may be true that these conditions are not met with very frequently, but an occasional single death caused by poisonous milk will be more than enough. Therefore, the daily home sterilization is by far preferable to the risky purchase from wholesale manufacturers who cannot guarantee because in the nature of things they cannot know the condition of their wares.

Another alteration of a less dangerous character, but far from

being desirable, is the spontaneous separation of cream from sterilized milk which is preserved for sale. Renk [16] found that it took place to a slight extent during the first weeks, but later to such a degree that 43.5 per cent. of all the cream contained in the milk was eliminated.

Sterilization has been claimed to be no unmixed boon because of its changing the chemical constitution of milk. Still, opinions on that subject vary to a great extent, the occurrence of changes being both asserted and denied by apparently competent judges. But what I have said a hundred times is still true and borne out by facts—viz., that no matter how beneficial boiling, or sterilization, or pasteurization may be, it cannot transform cow's milk into woman's milk, and that it is a mistake to believe that the former, by mere sterilization, is a full substitute for the latter. It is true that when we cannot have woman's milk we cannot do without cow's milk. There is no alleged substitute that can be had with equal facility or in sufficient quantity. But after all it is not woman's milk. Babies may not succumb by using it, and may but seldom appear to suffer from it; indeed, they will mostly appear to thrive on it; but it is a makeshift after all and requires modifications. Hammarsten was the first to prove the chemical difference between the casein of cow's and woman's milk. Whatever was known on this subject at that time I collated in Gerhardt's "Handbuch." [13] The casein of woman's milk is not so easily thrown out by acids or salts as that of cow's milk, and is more readily dissolved in an excess of acid. But lately Wroblewski demonstrated the difference in solubility of the two milks. Woman's casein retains, during pepsin digestion, its nuclein (proteid rich in phosphorus) in solution, it is fully digested; in cow's casein the nuclein is not fully digested, a "paranuclein" is deposited undissolved and undigested. Besides, woman's casein contains an additional albuminoid which is not identical with either the known casein or albumin (H. Koplik [14]). Of the albuminoids in woman's milk sixty-three per cent. is casein, thirty-seven per cent. lacto-albumin (Schlossmann), which being directly absorbable constitutes an essential difference from cow's milk; all of the latter has to be transformed during the digestive process before it can be assimilated. Besides, there is (Wroblewski) in the human milk another proteid rich in sulphur, poor in hydrocarbon, and, according to several authors, in albumoses and peptones.

K. Wittmaack and M. Siegfried [17] published lately their essays on nucleon (the phosphoric acid of muscle) in the milks of cow, woman, and goat, and on phosphorus in the milks of the cow and the woman. Their conclusions are accepted by E. Salkowski as correct, which, I should say, proves them to be so. Cow's milk contains 0.057, goat's milk 0.110, and woman's milk 0.124 per cent.

nucleon. In cow's milk the phosphorus of the nucleon amounts to six per cent. of the total amount of phosphorus contained in the milk; in woman's milk 41.5 per cent. That means that in cow's milk not one-half of its phosphorus is in the organic combinations of casein and nucleon; in woman's milk almost all of it is. In cow's milk the phosphorus not utilized for organic combinations is contained in the inferior phosphates. E. Salkowski adds the following remarks: "These conditions are evidently of the greatest moment in the nutrition of the nursling. As the development of bones is more readily accomplished in nurslings fed on woman's milk than in those fed on cow's milk, the probable conclusion is that nucleon has an important part in the absorption and assimilation of phosphorus." The same should be said of calcium, which also combines with nucleon. Though woman's milk contains less calcium than cow's milk, more calcium is utilized out of the former, and the nucleon is evidently an important factor in its absorption also.

Ergo, cow's milk is not woman's milk. It is not identical with it. Sterilization does not change its character; it merely obviates such dangers as result from the presence of most pathogenic germs and from premature acidulation. The substitution of cow's milk or of sterilized cow's milk for woman's milk as the *exclusive infant food* is a mistake. Experience teaches that digestive disorders, such as constipation or diarrhœa, and constitutional derangements, such as rachitis, may be produced by its persistent use, and it appears to be more than an occasional (at least coöperative) cause of scurvy.

Since the advisability of finely dividing and suspending the casein of cow's milk and of adding to the nutritiousness of the latter caused me always to advise the admixture of cereals with it, even in the very first days of infancy, the subject of infant feeding has never been lost sight of by medical men, scientists, and tradesmen. No subject has been treated more extensively, more eagerly, sometimes even more spitefully, than that of infant feeding. The philosopher's stone has not been so anxiously sought for nor so often found as the correct infant food and the appropriate treatment of cow's milk in medical journals, books, and societies.

The debilitating influence of persistent summer heat may be counterbalanced by improving the vitality and resisting power of the young. It is true no newly born baby should be bathed in cold water, but the gradual diminution of the temperature of the water used for ablutions may go on until after a few weeks or months the healthy infant bears washing and friction with cold water perfectly well. In the heat of the summer it should be so treated several times

a day. The clothing should be quite thin; those who perspire freely should have no linen next to their bodies; altogether, cotton or thin flannel, both of which gradually absorb and give off perspiration, are preferable. In very warm weather a single loose gown should be sufficient. No feather beds or pillows should be permitted. Surely the baby would be better off in a hammock, the head being supported by a hair or air pillow. Babies in bed should have their positions changed from time to time.

The mouth of the newly born infant requires the utmost care. It is a frequent inlet of microbes and toxins, and when its mucous membrane is injured, it adds a new element of danger to the different forms of intestinal and septic disturbances which are not at all uncommon at the earliest age. The attempts at cleansing the mouth may prove dangerous. All the integuments of the newly born are in a condition of desquamation. Clumsy rubbing with coarse or stained cloths by the fingers of a nurse or doctor that are not absolutely aseptic, is a direct cause of infection. Even the water in which the baby is bathed may add to that danger. What is called Bednar's aphthæ is nothing but the ulcerations of the very thin mucous membranes mainly on and near the alveolar processes; these heal but slowly and complicate every disorder of an infectious nature. If such a mouth is filled with sugar, teas, or syrups of questionable composition, the consequences are often bad.

Cow's milk will always be one of the foods administered at any age. In the country, when the cattle is not tuberculous, and when no diphtheria, scarlatina, and typhoid fever can vitiate the milk, it should be given fresh, modified by the addition of barley or oatmeal water. City milk is no longer fresh. In many medium-sized European cities milk is delivered within four hours after milking (in Frankfort for instance, since 1877); in New York it takes from ten to sixteen hours, or more. No such milk, unchanged, is fit for the use of young infants. Boiling, sterilization, or pasteurization is therefore indispensable, partly to destroy the bacterium aërogenes, partly to render innocuous such pathogenous germs as may have been admitted during the long time which elapsed between milking and consuming.

Even if it were possible to compound an accurate substitute for breast milk, this has the advantage of its freedom from pathogenous germs, and of its changeability under divers circumstances. Alterations of breast milk depending upon moderate changes of food taken by the mother or wet-nurse are as a rule not hurtful; its dilution by the ample quantities of water taken by them in hot weather is a direct advantage to the nursling. The same quantity and quality of food is

not equally digestible in summer and in winter; what is well borne and demanded in the winter, by the adult or by the young, proves an excess in summer. "Modified milk," "Gaertner's milk," and their like are always the same, day in and day out; breast-milk, however, may change. The main danger attending the uniformity of food is, in hot weather, the insufficient amount of water, of which our babies do not receive enough. Casein, sugar, fat, and salts should not only have their due average admixture of water, but the latter should be given in extra doses during hot weather. Perspiration thickens the blood, hinders the circulation, and may even lead to thromboses; it is good practice, therefore, to give breast-fed children a drink of water—which should be boiled and thereby sterilized—before each nursing; and to dilute the artificial food given to those who are brought up on the bottle, and to let them all have water between meals to their heart's content.

Treatment.

The most perceptible symptoms of cholera infantum are vomiting and diarrhœa, both of which are in the large majority of cases—to say the least—the effects of irritation or paralysis caused by bacteria and toxalbumins. Whatever is still within reach and active, should be removed by irrigation. If there is reason to suppose that the stomach still contains foreign materials, it should be washed out, no matter whether the attack is attended with fever or not. Both bacteria and toxalbumins may prove fatal without much increase of temperature; indeed, many attacks of cholera infantum behave in this respect like diphtheria, puerperal fever, or other septic processes, the worst forms of which are often accompanied with low temperatures. A mouth gag is not always required for the purpose of irrigating the stomach, but in most cases it facilitates the procedure; a cork firmly planted between the alveolar processes will generally suffice to enable the fingers to perform their work. No solid stomach tubes should be employed. Soft elastic catheters, Nos. 16 to 30 French, according to age, will suffice. The baby, wrapped up in a blanket and sitting on the lap and between the arms of an attendant, is satisfactorily immobilized, and its head is sufficiently fixed and bent forwards so as not to narrow the space between trachea and vertebral column. There are but few cases in which the œsophagus is missed at the first attempt; when the tube has once entered, the slight contraction behind the larynx is easily overcome, and the catheter slides down. By means of a glass tube and an india-rubber tube attached to it, the connection with a funnel, through which tepid water is

slowly poured in, is easily established. The flow is graduated by the elevation of the funnel. When a few ounces have been allowed to fill the stomach, the funnel is lowered and the liquid runs out. The same procedure is repeated, while the amount of liquid is increased, until the water returns clear. Vomiting alongside the tube is not harmful. The "fountain syringe" in common use among us will answer every purpose. In individual cases, when the indication of direct disinfection appears urgent, the tepid water (or 0.6 per cent. salt solution) may contain resorcin (one per cent.) or thymol (.02 per cent.) or permanganate of potassium (.02 per cent.). As a rule these additions will not be required; nor is the irrigation of the stomach indispensable when the patient is seen some time after the vomiting has ceased. In bad cases, however, any doubt in that respect should be dismissed in favor of irrigation. It will not often be required a second time.

The next step in the treatment of cholera infantum is the washing out of the intestinal tract as far as it is accessible. The fluid to be introduced is the same as above. In a number of instances when there seemed to be intense pain or tenesmus, I have mixed subnitrate or subgallate of bismuth with the water. The baby should be placed on one side, the nozzle of the fountain syringe introduced a few inches, and the instrument suspended a foot or two over the anus. To facilitate the flow, the hips should be somewhat raised; in some instances the gentle manipulation of the abdomen answers the same purpose. To introduce a long tube in order to reach the colon is either unnecessary or contraindicated. For in the infant the sigmoid flexure is so long that no tube passes the convolutions which are apt to cover one another, and sometimes reach to the opposite side of the upper pelvis. When the temperature of the body is high, the injection should be cool; when there is collapse, it should be hot. In the latter case, a small amount of alcohol (one per cent.) or good brandy or whiskey (two or three per cent.), or coffee should be added to the injection. These irrigations should be continued until the fluid returns clear; they should be repeated when the diarrhœa returns, and particularly when the stools are offensive. That all the injected fluid should be expelled is not necessary; on the contrary, as the loss of organic water has been great, and some of the dangers of cholera infantum depend on that very loss, it is desirable that the intestine should retain and absorb some fluid. That loss is so serious indeed that the introduction of water becomes an urgent necessity. To fulfil this indication in emergency cases, subcutaneous infusions of salt water (6:1,000), with or without the addition of sodium carbonate (10:1,000) are required. The water,

however, should be sterilized, and the whole procedure must be aseptic. It is true that many of the cases which indicate it will die; but it is not the infusion, but the disease that kills. I feel certain that a few of the patients I have seen the last half-dozen years were thus saved.

In connection with the question to what extent disinfectants added to the irrigations destroy bacteria or other toxins, I should state here that this effect need not be accomplished and still salutary action may be obtained. Many years ago Prudden proved that a one-twentieth of one per cent. solution of carbolic acid annihilates the action of bacteria, not indeed by killing but by paralyzing them. To prevent them from evolving toxins is as beneficial as to destroy them.

The same remark should be made in regard to those internal remedies which appear to be indicated, mainly in those cases which owe their origin to, or are evolved out of any of the forms of prodromal enteritis or enterocolitis, for the purposes of disinfection. Vaughan believes that much harm and no good can be obtained from them, but every clinician knows that the eminent bacteriologist is mistaken. It is true that calomel, naphthol, naphthalin, salol, and camphor in medicinal doses do not diminish the number of bacteria, not even of saprophytes, but the effect of the microbes becomes less virulent.

Constant vomiting forbids the introduction of food or drink. Whether there be thirst or not, the patient must be starved. While he is so deprived his thirst will decrease rather than increase. This period of total abstinence may last from four to twelve hours. After this some bear small pieces of ice quite well; but to begin with it too early excites vomiting and peristalsis. A teaspoonful of boiled water, cooled, may be given every five or ten minutes. That may be alternated with, or replaced by thin and thoroughly cooked and strained barley water. It is unirritating and well borne. What a critic" of Pepper's text-book says, viz., that "thousands of children are killed by the injudicious" (?) "use of barley water"—that this is "a popular fallacy" and "merits oblivion," is a mistake and reads like a huge joke. Later on egg water may be given, that is the white of a fresh egg beaten up, and finally shaken in a bottle containing 150 or 200 c.c. of barley or rice water, in small amounts.

No milk must be given at this stage; no sterilized or pasteurized milk, no breast milk. It is true that under ordinary circumstances milk feeds babies, but in these extraordinary circumstances it feeds bacteria. No milk must be given, if it take a week or more, until the alvine discharges begin to change, and are no longer malodorous. Now and then a teaspoonful of a mild tea, or a few drops of a good whiskey in barley water may be given once every five or ten minutes, or at longer intervals. A mixture which has served me well in many

cases, after the starvation period had passed and the stomach began to exhibit some little tolerance, is the following: One hundred and fifty cubic centimetres of barley water, the white of one egg, one or two teaspoonfuls of whiskey, some salt and cane sugar to improve the taste. Of this a teaspoonful is administered every five or ten minutes.

When milk is to be fed again, it should not exceed ten per cent. of the barley water with which it is to be mixed. To prepare it with hydrochloric acid, according to the prescription of Dr. Rudisch which I have frequently used these more than twenty-five years, will often be found profitable. The method is to mix 2 c.c. of *dilute* hydrochloric acid with a pint of water and to add thereto a quart of milk. This is to be boiled. If ever there be coagulation, it merely proves that the acid was mistakenly used in excess.

Internal medicinal treatment is mainly indicated in those cases which developed on the basis of a dyspeptic, catarrhal, or follicular enteritis. As irrigations of the rectum act on the lower part of the bowels only, the small intestines may be cleared by a purgative. If castor oil be retained, it will have a good effect. To mix it with tincture of opium is unwise at that stage in which the emptying of the tract of injurious masses is the main indication. Calomel may take its place, and will be well tolerated in frequent (hourly) doses of 4 to 5 mgm. (gr. $\frac{1}{15}$ to $\frac{1}{12}$). It should be continued until the stools show its effect, which they will do though the remedy remain in the mouth and be there absorbed after having been transformed into a mercurial albuminate. If there be an excess of acid (lactic, acetic, or butyric) in the stomach, calomel should be combined with an alkali, mainly chalk, the carbonate and phosphate of which have the additional advantage of forming with the fat an insoluble combination which acts as a protective cover to the sore mucous membrane. Doses of from 5 to 10 cgm. (gr. i.–iss.) may be given every two hours. The subnitrate, the subcarbonate, or the subgallate of bismuth in doses every two hours of from 15 to 100 mgm. (gr. $\frac{1}{4}$–iss.) acts as a disinfectant, partly by binding sulphide of hydrogen, and protects the sore surfaces. Salol should not be given in larger doses than from 3 to 15 cgm. (gr. ss.–iiss.), resorcin from 15 to 30 mgm. (gr. $\frac{1}{4}$–$\frac{1}{2}$.). These are preferable to many others because of their indifferent taste. When the time has arrived for astringents, nitrate of silver in solution, 2 to 4 mgm. (gr. $\frac{1}{30}$–$\frac{1}{15}$) in a teaspoonful of water, or gallic acid in doses of from 5 to 15 cgm. (gr. i.–iiss.), or tannalbin or tannigen, in doses of from 3 to 12 cgm. (gr. ss.–ii.)—all of them in intervals of two hours—may be administered.

Are there any indications for opium, or is it totally contraindi-

cated? It certainly limits secretion and hyperacidity better than morphine. Its effect is slower than the latter, and therefore safer and local. It also diminishes hyperperistalsis; it is, through its effect on the sensitive nerves or on the ganglia, a sedative, and an inhibitory agent through strengthening the splanchnic. Finally it relieves pain. Thus it is readily seen that in the incipient stages of dyspeptic and stercoraceous diarrhœas it finds no place, but when the bowels are emptied, it fulfils its indication of relieving pain and hypersecretion and of stimulating—in small doses—the heart. Under these conditions a baby of six months may take from four to ten drops of the camphorated tincture of opium, or an equivalent, every two, three, or four hours.

Great sensitiveness of the abdomen may also be relieved by warm fomentations, with water, or with poultices. They should be covered with oiled silk, or an india-rubber cloth and flannel. Care should be taken lest the clothing and bedding get moist. Warm bathing may occasionally take their place. In cases of collapse the temperature of fomentations or baths may be raised a little beyond the normal temperature of the blood. When there is great pain combined with high temperature of the body, cool applications to the abdomen are indicated. The cloth wrung out of cool water, secured and protected as above, should be changed when it becomes hot.

Great care should be given to the relief of the exhausted and paralytic condition of the patient. There are those cases which require stimulation at once. It is indicated when the fontanelle is depressed at an early time, the pulse very small and frequent (150–220) and hardly perceptible at the wrist, and the complexion ashy. To rely on internal stimulants is out of the question; there are, however, many opportunities for subcutaneous applications of the salicylate (or benzoate) of sodiocaffeine, of the sulphate of strychnine, of camphor, or of whiskey. The first may be employed in doses of from three to eight drops of the saturated solution (1:2), the second in doses of from 0.5 to 1 mgm. (gr. $\frac{1}{120}$—$\frac{1}{60}$), the third in doses of from four to ten drops of a solution in four times its weight of sweet almond oil; of the last from fifteen to twenty-five drops may be injected. All of these administrations may be repeated according to indications. The same remedies may be used internally if the condition of the stomach permit. The very best stimulant is Siberian musk, of which from 3 to 10 cgm. (gr. ss.–iss.) may be given every half-hour, until from three to six doses will have been taken.

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CHOLERA NOSTRAS.

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CHOLERA NOSTRAS.

AFTER the diarrhœal disease, epidemic in India, found its way into other countries and became known as "cholera indica" or "cholera asiatica," it became necessary to designate another disease, having a like clinical picture, but not originating in India, by a distinctive title. Thus different names sprang into use; of these, the name "cholera nostras" seemed to be the most appropriate. The designation of the indigenous cholera as "European" or "sporadic" is inappropriate, for the former name postulates incorrectly a special disease of similar nature for each of the different divisions of the globe, and the name "sporadic" does not fit in with the fact that there may be many cases of the disease occurring at the same time.

History.

Disturbances of the gastrointestinal function, through the taking of improper food, have been known of old; yet the precise period when the disease known as cholera was first described in literature seems doubtful.

The prescriptions and earnest demands for moderation in the book of Jesus Sirach are more of a general nature than of any special application to cholera. Hippocrates, at any rate, mentions clinical pictures which can be looked upon as those of cholera nostras. Celsus, Cælius Aurelianus, and Aretæus are said to have described the disease. I find a very accurate and surprising account of cholera (ἀπὸ τῆς χολῆς) in Forestus, though the clinical picture of Riverius is somewhat doubtful.

In the years 1669, 1674, 1675, and 1676, Sydenham observed epidemic diseases, whose prominent symptoms were diarrhœa, vomiting, feeling of anxiety, cramps of the legs and arms, coldness of the extremities, and often a fatal course in twenty-four hours. In this description, the frequent occurrence of intense cramps of the whole muscular system is noteworthy.

From the description of several later epidemics of the eighteenth century, which began with abdominal pain and constipation, Lebert is disposed to attribute them to lead colic, as lead was much more

likely to be present in the food then than it is now. Epidemic occurrence, in the sense that whole families and houses were attacked, has certainly become less frequent in the course of time. The cases are mostly sporadic, though indeed many persons are sometimes attacked simultaneously.

Several districts are described as places of predilection for the disease. According to the reports of Hirsch, the countries of the Northern continent are favorite sites, as opposed to those of the Southern continent. The disease is mentioned as being particularly frequent in North America, where every year in late summer and autumn a large number of people—especially children—are attacked. The larger European cities, too, show a not unimportant number of deaths from cholera nostras in children, though the better preparation of milk and the better facilities for good drinking-water in the cities seem to have favorably affected the number of cholera nostras cases in the last few years. The severe types of the disease among adults ought to be less frequent than formerly, because of the present sanitation of city and country.

With the occurrence of Asiatic cholera outside of India it became difficult to differentiate the two diseases. If the Indian cholera were not characterized by its epidemic spread and its high mortality, differentiation in many cases between the two would be extremely difficult, even impossible.

In consequence of the recent discovery by Koch of the comma bacillus a change has taken place; yet even now there are some questions pressing for solution. At any rate, it is surprising to observe the frequency with which cholera nostras has occurred in the midst of epidemic cholera, and to observe how, towards the end of an epidemic of Asiatic cholera, a milder epidemic, consisting of cases of cholera nostras, takes place. In this connection, experiences in Livorno and Lisbon are recalled. Similar pictures were observed in 1893, 1894, and 1895, and were described by Gotschlich.

Etiology.

This disease differs etiologically from Asiatic cholera, that is, the vibrios discovered by Koch are not found either in the dejections or in the intestinal canal in cholera nostras. A distinct cause for the occurrence of cholera nostras cannot, however, be proved.

The disease occurs most frequently during the hot season of the year, particularly in the latter part of summer, so that it has been called "summer diarrhœa" by American authors. Cases, however, do occur in autumn and even in winter, being then generally caused by

food, in which it is either supposed or proved that decomposition or noxious admixture has taken place. If these noxious substances find their way into the intestinal canal of a large number of people, then groups of cases of greater or lesser dissemination occur.

Naturally, decomposition of food takes place more frequently in hot weather than in winter. The explanation of this fact is that these decompositions occur through the action of schizomycetes which require for luxuriant growth a certain amount of warmth. That, however, even without the schizomycetes, poisonous substances may be found in the food, and give rise to cholera nostras, has been shown by those cases occurring after the use in bread-baking of certain prepared mineral oils which have petroleum as their base (Dunbar). The question whether fish- and cheese-poisoning can occur without the action of schizomycetes requires further investigation.

However, in many typical cases of cheese-poisoning running the course of cholera nostras, the schizomycetes have been searched for very often and not found; there is only one case recorded in which a hyphomycete is said to have been discovered. Nevertheless, the many microorganisms existing in cheese make more probable the origin of the poison through the action of these bacteria, than otherwise.

Fish-poisoning can more probably occur without bacterial influence than cheese-poisoning; at any rate, typical symptoms of intoxication can be produced by certain kind of fish, in which even the fresh organs already contain the poison. This intoxication may find its analogy in that of mussel-poisoning so thoroughly described by Schmidtmann, in which the poison is preformed in the liver of the mollusk. However, the clinical picture of the sickness resulting from the above-described fish-poisoning is that of paralysis rather than of cholera, and the great majority of cholera nostras cases are probably caused by the fact that the fish either is already in process of decomposition or contains living schizomycetes. In this connection the work of Ziber is of interest. He discovered the bacillus piscicidus agilis which he gives as the cause as one form of fish-poisoning, and he also found the same bacillus in the stools of two fatal cases having symptoms similar to cholera. The cases of cholera nostras which now and then occur after eating oysters are probably to be explained in similar manner.

In general, the same observations are true for meat-poisoning. Here too, an analogy with belladonna poisoning may be thought of, in that the animal during life assimilates poisonous substances without harm, which substances, after the animal is killed and eaten, may cause disease. Recently, Alt has traced cases of infantile diarrhœa

to the milk of cows which had been fed on diseased clover; yet such a cause of cholera nostras cannot be frequent.

On the other hand, the cause of severe illness following the ingestion of meat has very frequently been found to be microorganisms. The most severe form is that due to intestinal infection by anthrax, caused by eating meat containing this bacterium; as a result is produced a disease resembling cholera. It will, however, be necessary to differentiate this fatal disease from cholera nostras; even though there is a clinical resemblance between them, the etiological factors are easily seen to be different in the two cases.

We must differentiate from cholera nostras also certain forms of meat-poisoning which are not manifested by gastroenteritis, but present certain toxic symptoms, such as salivation, paralysis of the external and internal eye muscles or of the muscles of deglutition, or respiratory or cardiac symptoms. We have to do in these cases with the presence of special forms of microorganisms which have already split up the proteids of the meat before its ingestion and have formed very powerful toxins. Von Ermengen has recently described a new anaërobic bacillus as one of the agents concerned in the formation of toxins of this sort. Poisoning of this kind is very different from that caused by the pathogenic microorganisms of gastroenteric disorders.

With the advance of bacteriology during the last few years, the etiological factors of cholera-like diseases have been diligently sought after. Finkler and Prior (in 1884) found, in a small epidemic of cholera nostras at Bonn, a small cholera-like spirillum in the dejections, which spirillum they considered the cause of the diarrhœa. A similar spirillum was discovered by Holst, but the report of Ruete and Enoch as to a similar discovery was later rectified, the microbes described by them having been found to be true cholera bacilli. Meyhöffer has found a bacillus which rapidly liquefies gelatin and causes a bad odor, while Hueppe has found in the rice-water stool of indigenous gastroenteritis short bacilli which do not liquefy gelatin and which he classed with the typhoid group. Fischel and Enoch got a culture of small liquefying bacilli from a carp which had ecchymotic areas; the boiled flesh therefrom caused vomiting and diarrhœa when fed to dogs.

Gärtner found, in the meat of a slaughtered cow which caused sickness in fifty-eight people who had eaten it, a bacillus which does not liquefy gelatin; he called it bacillus enteritidis. This same bacillus Günther found to be the cause of cholera nostras which had attacked twenty-six or twenty-seven families in the province of Posen. Gaffky and Paak isolated from sausages which had produced cholera nostras a motile bacillus: this bacillus produced diarrhœa and death

in apes. Baginsky found the proteus vulgaris in the dejections of nursing children having diarrhœa. Klein looked upon a similar form as the cause of meat-poisoning. Karlinsky discovered in dried goat's meat, which when eaten had sickened many persons, the bacillus of Gärtner; similar observations have been published by von Ermengen and Lubarsch.

Most authors have found the bacterium coli either in pure cultures or mixed with other forms. Bleisch and B. Fischer have isolated a cholera-like spirillum which they regard as the cause of cholera nostras. Peculiar cholera-like bacilli were also found by Dunbar and Vogler in the waters of the Elbe and other rivers flowing through districts in which choleraic affections had occurred. Since these bacilli could cause diarrhœal diseases, and since, by the methods then known, these bacilli could not be differentiated from the spirilla of true Asiatic cholera, it was naturally thought that these, too, were genuine cholera spirilla. Later, Kutscher, and simultaneously, Oergel and Willgerodt, observed that some of the spirilla found by Dunbar in river water had the power of phosphorescence.

Rumpel, who claims to have seen phosphorescence in the true cholera bacilli, believes there exists a connection between these spirilla and the microorganisms of Asiatic cholera. Most authors, however, regard them as belonging to a widely spread family of indigenous summer and autumn fauna. At the beginning, a relation between cholera nostras and Asiatic cholera must have been supposed to have existed, for some cases, having phosphorescent bacilli in the stools, had a symptomatology similar to that of true cholera, and these mild cases may have been thought to be cases of either true or doubtful cholera. Pfeiffer's discoveries, however, have shown that these spirilla have no connection with those of true cholera indica.

Recently the presence of spirochætæ, which also occur less frequently in Asiatic cholera, has been observed by many. Probably in both diseases the presence of these forms is of minor importance. In Hamburg, in 1892, these microbes were observed in one case of true epidemic cholera.

Gottschlich, in 1893, 1894, and 1895, made a similar discovery in the stools in several cases of severe gastroenteritis occurring in Silesia. Bacilli were found very similar to those of cholera, but they did not respond to the nitroso-indol reaction.

Carp describes a small epidemic of cholera nostras occurring in Wesel, in which no cholera bacilli were found, but in which five cases out of six died. Since at this time there were cases of true cholera in the Rhine provinces, this observation of Carp is somewhat doubtful.

Kaensche examined, in the Hygienic Institute at Breslau, samples of beef which had caused symptoms of cholera nostras in eighty persons, the disease having been at times accompanied by fever, dizziness, fainting spells, and herpes. These samples of meat, when fed to animals, produced severe intestinal hyperæmia, punctate hemorrhage, and transudation into the intestine; the animals died with paralytic symptoms. Bacteriological examination showed the presence of a short, narrow bacillus, very motile in the hanging drop, with many flagella which were easily stained by aniline colors and decolorized by Gram's method. In bouillon culture, the bacteria showed the indol reaction, and in agar containing grape-sugar they gave rise to the formation of much gas; on gelatin plates they grew like typhoid bacteria.

Pottien found, in a case of cholera nostras which ended fatally, besides a virulent bacterium coli, a microorganism of great motility which had the power of producing a pigment. Since this organism also had the power of forming capsules when in the bodies of animals and in all culture media except milk, he called it bacillus fluorescens capsulatus. He differentiated it from bacillus pyocyaneus. When animals were inoculated with the bacillus fluorescens, the intestinal canal was attacked. As Pottien found the same bacillus in two cases of cholera nostras, he was led to look upon it as the cause of the disease. Very recently, Klein has described as a cause of severe diarrhœa a cylindrical, motile bacillus, with long flagella, which grows only when air is excluded. This bacillus was discovered in an epidemic caused by infected milk, occurring in St. Bartholomew's Hospital, London.

During 1893, 1894, and 1895, 137 cases of cholera nostras were received in the New General Hospital in Hamburg. The reason for this large number of cases was the watchfulness of the authorities and the necessity of minutely examining every case resembling cholera. Of these 137 cases, 114 were received in 1893 alone. One would naturally think that this was due to the warning of authorities and physicians; yet it is noteworthy that, in the total population of Hamburg, there were in 1893 620 cases, in 1894 197 cases, and in 1895 186 cases of vomiting with diarrhœa reported, so that these indigenous cases of gastroenteritis occurred more frequently at the end of and contemporaneously with the outbreak of Asiatic cholera than before it.

In all these gastroenteric cases, a thorough bacteriological examination was made. It is remarkable to observe how rich were the stools, when freshly examined in the hanging drop, in bacteria of the most varied kinds. There were found forms of small size and great

motility which Wieniorowski has compared to a swarm of gnats; there were non-motile, large and small bacilli, often curved; and cocci. A cover-glass preparation of fecal matter, freshly stained, very often showed this same bacterial richness.

As opposed to this variety of and richness in bacteria, gelatin plate cultures containing one per cent. peptone-salt solution, and other gelatin plates inoculated from these, showed only a moderate number of bacterial forms.

Rumpel has tabulated these observations, made in the New General Hospital at Hamburg. There were found:

	Nothing special.	Bacterium coli.	Proteus vulgaris.	Powerfully liquefying forms.	Bacillus Bleisch.
In 25 cases of diarrhœa	11	7	2	4	1
In 62 cases of gastroenteritis	22	26	7	5	2
In 39 cases of cholera nostras	16	10	9	3	1
Total	49	43	18	12	4
Percentage	39	34	14	10	3

Recently my assistant, Dr. Fricke, has discovered a capsulated bacillus in four cases of cholera nostras. It appears in the form of very large non-motile rods with rounded ends, acquiring capsules in the living body and, at the beginning, in culture media. These rods are decolorized by Gram's method, and show a rapid formation of gas on agar.

A dog fed with a pure culture of this capsulated bacillus had diarrhœa, with severe general symptoms. After the recovery of the animal, another feeding of the bacillus produced diarrhœa for a short time only.

If we sum up the results of these examinations, we must conclude that no single etiological factor for cholera nostras exists.

In about three-fourths of the cases, the ordinary intestinal bacteria or bacteria coli are found almost in pure culture. Besides there are often found proteus forms, as described by Hauser. We were at first inclined to attach great importance to this form; but it has now been found that we can grow them as we can the bacteria coli in cultures from the normal intestinal contents.

Special interest, too, was at one time attached to the bacillus Bleisch, the colonies of which in gelatin plates and gelatin stab cultures very much resembled those of the cholera spirillum, and which very often formed a pellicle in peptone water. This bacillus was, however, found in only a small percentage of cases. The same may at present be said of the bacillus capsulatus, of which Fricke

found a non-motile form and Pottien a very motile, fluorescent form.

It might be thought that certain of these, at times with difficulty differentiable forms are particularly virulent or might become so under favorable circumstances, and so produce the disease. However, it can with equal justice be assumed that the bacterium coli and the proteus increase very rapidly and become very virulent as a result simply of digestive disturbances.

Yet the multitude of the different microorganisms, whose connection with the later occurring disease can be demonstrated, leads to the conclusion that cholera nostras has no single etiological factor, but that the most varied microorganisms can form, in articles of food, those toxic substances which produce the clinical picture of cholera nostras. The condition of the body ought also to be considered, as shown by Fricke's experiments. At any rate, we have to deal with the most varied forms, a great part of which we do not as yet know, just as the most varied chemical substances and poisons may produce the same symptoms. Among these substances I need mention only colchicine, solanine, and the arsenical preparations.

The greatest number of cases of cholera nostras occur, as already said, during summer and autumn, at which times the natural warmth favorably affects the development of bacteria in food and drink. If the amount of either the microorganisms or the toxic substance introduced into the body be not too large, severe illness need not necessarily follow.

The chances of illness increase when a certain amount of weakness of the gastrointestinal tract exists, this weakness being at times called forth by dietetic errors; in such a condition, overloading the stomach with food difficult to digest, drinking cold beer or bad drinking-water, the taking of ice, one or all may act as exciting causes. Cold applied to the abdomen, as well as strong emotions, likewise increase the predisposition to cholera nostras and cholera asiatica.

In consequence of individual idiosyncrasy, some people are very sensitive to the disease and suffer an attack on the slightest provocation. Now and then the same cause acts upon a larger number of people, and thus arise many cases of gastroenteritis. In this connection, the use of bad drinking-water is of first importance. In the New General Hospital at Hamburg cases of summer gastroenteritis, following drinking of the Elbe River water, are often met with at times when epidemic cholera does not exist.

A direct or indirect contagion of cholera nostras from one person to another has never been positively verified. It is interesting to note that, along with an epidemic of Asiatic cholera, many

cases of non-specific gastroenteritis occur. In Hamburg also, towards the end of the epidemics of true cholera occurring in 1892 and 1893, there were many cases of cholera nostras, cases, at least, which, after a bacteriological examination continued for many days, did not justify the diagnosis of Asiatic cholera. During the mild and very carefully studied epidemic of cholera of 1893 in Hamburg, in which, besides 80 typical cholera cases with 44 deaths, and 60 cases of cholera diarrhœa, so-called cholerine (in 2 of which comma-shaped bacilli were seen, which perhaps should be regarded as identical with Dunbar's bacilli), there were observed 29 cases of cholera nostras with 2 deaths in the New General Hospital; the most careful bacteriological examination of these last-named cases failed to show the comma bacillus.

It is possible to think that with still more improved and thorough methods of examination of the future some of these cases of supposed cholera nostras will be found to be really Asiatic cholera, the comma bacilli, dead, yet just as poisonous, or the cholera poison alone being introduced into the gastrointestinal canal; or, as Rumpel thinks, the bacillus may have been killed in the body by the protective power of the organism. Yet we cannot regard all cases of cholera nostras, occurring in the course of an epidemic of Asiatic cholera, as of that nature.

It is possible also that certain otherwise harmless microbes which perhaps temporarily do not grow may sometimes acquire toxic properties under the influence of the same etiological factors of time and place as those of cholera indica, or under the influence of the cholera bacilli or cholera poison.

Symptoms.

In the symptomatology of Asiatic cholera, we find that the etiological factor has no effect on some persons, while in others it produces a simple diarrhœa, and in a third group it causes severe attacks of true cholera.

Without doubt, the same holds true for indigenous cholera. Particularly the cause may lead, in some, to diarrhœa only; in others, to typical diarrhœa and vomiting, accompanied by severe symptoms. In this connection, it may be stated that small children are most liable to be attacked. Here we see cholera nostras very often coming immediately after milder and, at the beginning, symptomless disorders of digestion, or, as Heubner very justly observes, a chronic digestive disturbance may pass over towards the end of life into a disease very much resembling cholera.

In adults, too, for one or more days, moderate diarrhœa with

nausea, abdominal pains, and flatulence may precede the real attack of cholera. In other cases, the beginning of the disease is very sudden. The initial symptoms are pain in the region of the stomach or in the abdomen, general malaise, nausea, and a feeling of anxiety. Soon symptoms of now gastric, now enteric disorder become most prominent. First eructations, nausea, and vomiting appear. The stomach is emptied of the food which it contains, without the latter having necessarily caused the disease; later the vomitus becomes watery, contains mucus, and is yellow or green, depending upon the greater or less admixture of bile. There is very often a bitter taste in the mouth, thought to be due to peptone from the intestinal canal. Now the diarrhœa soon begins. Generally this begins after the patient has experienced abdominal pains, though now and then these pains are absent.

However, this order may be reversed, the disease beginning with diarrhœa which is followed by the vomiting. The stools are brown, at first formed, later watery. The more frequently the stools follow each other the less are they colored, and hence very much resemble the rice-water stools of Asiatic cholera. Blood in the dejections is rare.

The diarrhœa and vomiting may follow each other with great violence, they may alternate or may occur simultaneously. The number of the often strong-smelling dejections may reach an alarming height; the passage of ten to twenty stools in twenty-four hours is not rare; the abdomen is generally very sensitive, most frequently soft and doughy, later sunken. Attacks of colic either accompany the stools or occur spontaneously. The feeling of oppression becomes greater and often has a character resembling that of angina pectoris. The tongue is generally thickly coated, and there is a bad taste in the mouth. Great thirst makes its appearance at this time. In a few cases all fluids are immediately vomited unchanged as in true cholera.

The more strongly marked are the individual symptoms, the worse as a rule does the general condition of the patient become. The patients grow faint and weak, blue rings form under the eyes, the face is shrunken, the pulse becomes more rapid and weak. Sooner or later a feeling of drawing and tension occurs, and cramps make themselves felt in the calves of the legs and in the feet; cramp-like pains also occur in other muscles and other portions of the body, particularly in the arms and fingers. Painful eructations and deglutition trouble the patients. With the increasing weakness the voice becomes husky, the respirations are more frequent, the skin is cold, cyanotic, and covered with clammy perspiration. Now we have a

picture which can hardly be distinguished from that of Asiatic cholera. The thread-like pulse and the frequently complete suppression of urine make the resemblance between these two forms of cholera almost complete.

In adults, this disease seldom causes death; but it terminates fatally in children more frequently. Sometimes with symptoms of oppression, at times with complete apathy, now and then with continued convulsions, the patients fall gradually into collapse, the eyes become sunken, the eyelids do not completely close, the lips and extremities become of a blue-gray color, and death follows, often quite suddenly.

Generally the disease terminates favorably; the violent diarrhœa becomes less, vomiting stops, and the stomach is able to retain fluids. Not rarely profuse perspiration occurs in the stage of convalescence. The more violent the initial symptoms were the greater is the patient's exhaustion on their cessation, and frequently this exhaustion leads to a refreshing sleep. If the disease has developed more slowly, so also is the restoration to health generally less rapid.

In both instances, great weakness remains for some time; there are general lassitude, weakness, and cramps in the legs (particularly in the calves), inability to work, etc. The gastrointestinal canal remains very sensitive.

In a few cases, as in Asiatic cholera, there is a stage of reaction. This reactionary stage may consist of a simple fever for some days, with continued gastric symptoms, thirst, dizziness, etc.; it may, however, lead to that clinical picture which we know as the "stadium comatosum" of cholera. The patient becomes delirious; the fever alternates at times with subnormal temperature; at the same time, the head and face are flushed, the pupils generally contracted; the corneal reflex may be absent, the skin is generally warm. Here, no doubt, we have to deal with secondary toxic effects, in which a certain flooding of the organism with the products of intestinal putrefaction, by reason of the damage to the intestine, probably plays an etiological rôle in addition to that of the toxin. The fact that a typical exanthem may develop during this coma, just as in that of true cholera, fits in with this view.

Rumpel has published among his observations in the New General Hospital at Hamburg an instance of the above. Here the exanthem occurred during the last day of the coma, and initiated a febrile stage which led to recovery. The exanthem lasted several days. Such an eruption, however, does not seem to be very frequent; and were it not for the fact that the most careful bacteriological examination gave negative results, and also that Asiatic cholera had been absent for

some years, the presence of an exanthem might lead us to think of an Indian etiology of the disease. This case was also complicated by an infection of the kidney. Tolasse describes a similar complication in a case which ended fatally. Affection of the kidneys, in greater or less severity, moreover, seems generally to accompany the violent cases of cholera nostras, in that here the excretion of urine is completely abolished or much lessened, with the development of profuse diarrhœa. The urine may contain albumin and epithelial casts; particularly is this the case when the urine is scanty and after temporary anuria. In the observations made on cholera nostras in Hamburg, albuminuria was observed in almost fifty per cent. of the cases; Wagner, too, has made the same observations.

As compared with that of Asiatic cholera, the course of cholera nostras is generally much shorter. In more than one-half of the cases, the disease (or its severe symptoms at least) lasts a few days or a few hours only, while true cholera, even in favorable instances, generally lasts several days. A further differential point lies in the mortality figures of both diseases. While in Asiatic cholera of moderate severity the mortality is more than fifty per cent., a fatal termination in indigenous cholera is comparatively rare. Taking the average of many cases, the mortality of the latter disease is less than ten per cent. Cases like those in Wesel, in which five out of six died, leave room for the suspicion that the disease was not indigenous gastroenteritis.

As a further diagnostic point between the two forms of cholera, it is to be noted that a clinical picture of very severe illness, corresponding to cholera sicca, with absence of or very little diarrhœa, has not yet been observed in cholera nostras. This may be due, as Rumpel observes, to the small number of studies made in this connection. It is, however, possible that the poisons produced by the bacteria of cholera nostras are less active than those of Asiatic cholera, and become active only when the body is very much weakened by profuse diarrhœa, or when, by loss of the intestinal epithelial covering, absorption of toxins can more readily occur. When this occurs, however, the disease enters upon a stage which clinically may belong to either of the two forms of cholera.

In the majority of the cases of indigenous gastroenteritis the violent and severe symptoms soon cease, and then convalescence sets in relatively rapidly.

The unfavorable cases, however, fully resemble true cholera. All therapeutic measures, hot baths, rectal injections, subcutaneous and intravenous infusions of salt solutions, produce but temporarily good results; these soon fail, the pulse disappears, the second heart

sound can no longer be heard, and death follows progressive coldness of the body or paralysis of respiration.

Little is known of the sequelæ of cholera nostras. Painless diarrhœa, indeed, may continue many weeks after recovery from an acute attack; and for a long time this diarrhœa returns after every attempt to feed the patients upon any diet but milk and broths. In some patients, there is a certain weakness of the gastrointestinal canal following an attack of cholera nostras. Neurasthenic symptoms also may follow an attack of cholera nostras, or a previously existing neurasthenia may be exaggerated.

Pathological Anatomy.

In the rare cases of death among adults, no specific lesions have as yet been discovered.

The body shows a certain similarity to that of a person dead of Asiatic cholera as regards the color of the skin, mucous membranes, and nails, as well as the tension of the muscles. The opened abdominal cavity also looks the same, quite often, in the two forms. Yet the serosa in cholera nostras does not show such an extensive and pronounced red color as is seen in Asiatic cholera. The injection of the blood-vessels most often appears only in streaks. Frequently small subperitoneal ecchymoses have been observed.

The mucosa of the stomach is much reddened, that of the intestines is often bared of its epithelium and studded with hemorrhages; the intestinal contents are generally only watery, odorless, and containing shreds of the desquamated mucous membrane. Tolasse has also observed sloughs in the colon.

Heubner has found marked microscopic changes. Even the stomach mucosa showed a partial degeneration of the superficial epithelium. The glandular and surface epithelium of the jejunum and particularly of the ileum showed, on the other hand, very marked changes. This epithelium was not completely thrown off, as in Asiatic cholera, but appeared as dull, cloudy, non-nucleated flakes in which no distinctly defined cells could be made out. Some of these glassy, flake-like masses contained vacuoles; in a few instances nuclei or traces thereof could be made out, yet they did not stain clearly, nor did the cell protoplasm stain as distinctly as usual. Besides these lesions there were found hyperæmia of the capillaries and œdema of the submucosa. Thus the changes of the intestinal epithelium are similar to, though by no means as pronounced as, those of Asiatic cholera.

The remaining abdominal organs in cholera nostras show marked

injection, particularly — as now and then observed — the kidney. The kidney cortex in these cases was swollen and cloudy. Microscopically there were found, besides scattered changes in the parenchyma of the kidney cortex, a similar cloudiness and swelling of the renal epithelium with partial degeneration of the same, just as we find in the kidney of cholera indica, though the changes were not of so intense a degree as in the latter. In a particularly severe case of cholera nostras occurring in an adult who died in coma, Tolasse asserts that he found the same marked anatomical changes of the kidney as are seen in Asiatic cholera. So this anatomical difference between the two diseases, as regards the kidneys, which was noted especially by Klebs, seems not to exist.

Diagnosis.

The diagnosis of cholera nostras presents special difficulties in the differentiation from cholera indica, when we are in the presence of an epidemic visitation of the latter disease. During the course of an epidemic of Asiatic cholera we must always remember the possibility of the occurrence of cases of cholera nostras at the same time.

It is to be noted at the beginning that the appearance of the stools alone shows a difference between the two diseases; and that severe illness due to indigenous cholera can be accompanied by the passage of light yellow-colored stools, while in severe cases of the Indian form I have almost never observed the absence of rice-water stools; yet in mild attacks of the latter disease colored stools do occur.

The premonitory diarrhœa of Asiatic cholera, formerly looked upon as a differential diagnostic factor, did not maintain its significance as such during the epidemic of Hamburg. There is thus hardly any other differentiation possible than the proof of the absence of the cholera spirilla.

It is, however, to be kept in mind that cholera indica generally attacks a greater number of individuals; that it is of decidedly longer duration than the indigenous form; that the mortality of the latter disease is a much smaller one; that in cholera indica the symptoms of intoxication generally appear after very profuse diarrhœa. All of these diagnostic points are particularly valuable in those places where cases of Asiatic cholera have not occurred for a long time, and where any connection with a centre of cholera infection can be excluded. However, all these diagnostic factors by no means make unnecessary a careful bacteriological examination.

The importance of this was well shown by the occurrence of a small epidemic of cholera, which broke out in the neighborhood of

Mayence in 1886, without any other known case of Asiatic cholera having occurred in Germany, and without the course of travel of the epidemic having been clearly made out.

Other diseases than cholera indica hardly come into consideration as regards the differential diagnosis. Since cholera nostras is a disease which can be produced through the most varied causes, it will always be the physician's task to seek for the etiological factor in the individual case or cases, whether this factor be the poison or poisons contained in the ingested food, or whether the disease has been produced *in situ* by the action of microorganisms in the gastrointestinal canal.

It is natural to recall that certain poisons, such as arsenic, solanine, and colchicine, can produce a condition similar to cholera nostras, and that these poisons may be given with criminal intent. In such cases, the diagnosis will be possible only by chemical examination of the vomitus or of the stomach contents.

We shall probably in the future learn to recognize a large number of poisons which can produce the clinical picture of gastroenteritis.

Prognosis.

We have seen above that cholera nostras only rarely causes death. This fatal termination occurs most frequently in children, the danger being greater the smaller and weaker they are. In the aged and invalids this disease also has its dangers; among such, violent and involuntary dejections of rice-water-like stools, collapse, small pulse accompanying a cold and clammy skin, cyanosis of the lips, ears, and fingers, are to be looked upon as *signa mali ominis*.

Strong individuals can withstand the apparently severest attacks. In such patients, improvement generally occurs in the most surprising manner, so that it is here necessary, despite the severity of the disease, to be guarded in making an unfavorable prognosis.

It appears, moreover, that some individual epidemics of cholera nostras are accompanied by higher mortality than others; thus, in the Hygienic Institute of Breslau, from 1893 to 1895 there were one hundred and seventy cases received from Silesia, with seventy deaths. The mortality of cholera nostras depends, no doubt, chiefly upon the degree of virulence and the quantity in each individual case of the exciters of the disease.

Treatment.

The first duty of the physician, in treating cholera nostras, is the removal of the poisonous substances from the gastrointestinal canal. Only rarely will it be possible for the physician to remove the cause

from the stomach by lavage or the exhibition of emetics, thus producing very rapid recovery. As a rule the disturbing elements have already passed into the intestines. It is thus the object of therapeutics to remove these products from the intestines and to prevent further absorption.

Since the patients are generally in the stage of intoxication when they come under the physician's care, rapid treatment is necessary. In the majority of cases, castor oil, from one to two tablespoonfuls, or calomel can be given, according to the patient's condition. In adults, calomel in doses of 0.2 gm. (gr. iij.), given once or repeated, may be prescribed; in children, calomel can be given in doses of 0.01 to 0.05 gm. (gr. ⅛ to i.). Since, in general, children bear calomel quite well, it will do no harm to give the above doses more frequently. Wood recommends the prescription of opium with calomel; I have had no experience with this combination, but I have doubts of the utility of opium in such cases in which we try to get rid of irritating material from the intestines by increasing the peristalsis.

Since the medicines given by the mouth are very often vomited, it may be necessary to empty the intestinal canal as much as possible by rectal enemata. For this purpose, we may employ soap-water, with or without the addition of castor oil, or simple boiled water, with the addition of glycerin (100 to 200 gm. = ℥ iij. to vi.). According to Genersich, rectal injections of large quantities of tannin solution (1:1,000) are useful. It is possible that the tannin may combine with the poisonous materials. The liquid to be injected is warmed to 40° C. (104° F.), and then poured into the irrigator; here and in the tub it cools to 38° C. (100.4 F.°). Then, with the least possible pressure, the fluid is allowed to flow into the rectum. Often the fluid becomes mixed with intestinal contents and is immediately returned; there is no reason in this, however, for not continuing with the injection after a short pause. In this manner it is often possible to introduce large quantities of fluid into the rectum, a part of which will remain behind, the greater part being mixed with intestinal contents and returned from the bowel.

During the employment of these enemata, however, symptomatic treatment must not be lost sight of. Two indications have come into consideration. The more important indication is the prevention of threatening paralysis of the heart. In many cases the pulse early becomes very small, only one heart sound is heard, the patient's skin is cyanotic. In such cases it is necessary to restore the circulation as rapidly as possible. Besides the warm enemata, which in this connection often give favorable results, the most important procedure is the hot bath, the patient being wrapped in woollen blankets imme-

diately after the bath. To this hot bath may be added, depending upon the quantity of water, 100 to 200 gm. (℥ iij. to vi.) of mustard flour, in the way described in the section on the treatment of Asiatic cholera (page 430). It is said that the mustard flour has a more powerful action when stirred in cold water before being added to the bath.

It is likewise judicious to give the patients small quantities of warm—or, if these be vomited, cold—drinks. With the carrying out of this medication, the second factor of the symptomatic treatment is to be kept in view, viz., the prevention of thickening and stagnation of the blood.

Generally the absorption of fluids is prevented by vomiting. If this be so, the stomach should be washed out whenever it is possible to do it, since no therapeutic measure stops the vomiting so quickly as this; particularly in children I have found this measure the best for the relief of vomiting.

If, for any reason, lavage of the stomach cannot be carried out (though this ought only rarely to be the case), the vomiting may sometimes be quieted by the swallowing of small pieces of ice or the giving of small doses of chloral hydrate:

℞ Chloral hydrate ..... 1 (gr. xv.)
Distilled water ..... 80 (℥ iiss.)
M. Sig. : One teaspoonful as ordered.

Resorcin is recommended in attacks of gastroenteritis after the following formula:

℞ Resorcin..... 0.5–1.5 (gr. viij. xxiij.)
Distilled water..... 100.0 (℥ iij.)
M. Sig. : One teaspoonful every two hours.

This should, however, never be given in well-marked cases of cholera nostras. The best drink is hot tea or coffee, with a small quantity of cognac (one to two teaspoonfuls to the cup), taken in teaspoonful doses. In a similar manner, liquor ammonii anisatus can be given, five to fifteen drops every one or two hours in barley water or gruel.

Now and then warm drinks cannot be taken. Then small pieces of ice or cold champagne should be tried. On the whole, however, we should be careful in the use of alcohol; often its favorable effect lasts but a short time. We may also try plain ice-water, which is in general to be preferred to the carbonated waters, since the latter, according to my experience, increase the vomiting. For cases of obstinate vomiting, Liebermeister recommends repeated small enemata of 80 to 100 c.c. (℥ iiss. to iij.) of chamomile tea, each containing five drops of tincture of opium.

In threatening collapse, hypodermic injections of camphorated oil should be given, the camphorated oil being preferable to alcohol in that it does not have any untoward after-effects. By all these methods, the circulation is often improved and—what is particularly to be desired—perspiration is produced.

In more obstinate cases the effect of the hot bath upon the circulation of the skin can be strengthened by repeating the bath often and by rubbing the skin during the bath; furthermore, after the patient has been enveloped in the woollen blankets, the retention of warmth can be increased by surrounding him with hot-water bottles or hot sand bags.

I do not know, from personal experience, whether the same results may be achieved in cholera nostras by a cold sponging at 12° C. (53.6° F.), accompanied with friction and rubbing and then envelopment in woollen blankets, as can be secured by the hot baths. I have always had doubts about the utility of further withdrawing bodily warmth in the case of a patient with subnormal temperature. However, it may be possible that the application of cold accomplishes the same results as heat.

As a powerful stimulant and irritant to the skin, in children, Lebert recommends wrapping the patient in a cloth which has been dipped in a strong mustard infusion, in addition to the use of the woollen blanket; the patients remain thus enveloped for one-half to one hour. This procedure is repeated several times during the day.

If all these methods fail us and the stage of asphyxia still continues, it becomes our duty to proceed to infusion without further delay. The intravenous infusion would here accomplish the quicker result; but in practice this procedure cannot very often be carried out, hence the subcutaneous infusion must be substituted; indeed, Hager ascribes better action to the latter. (See article on Asiatic cholera, section on treatment, page 435.) In a case of cholera nostras, Rumpel has recently tried to introduce large quantities of alkaline fluid into the stomach by means of the stomach tube, and then more rapidly forcing the toxins from the body by means of stimulating diuresis.

Generally, after recovery from an attack of cholera nostras, there are no sequelæ. However, recently we have observed cases in which there was as a sequel a condition resembling the comatose stage of cholera indica. Similar observations have been made by Griesinger and Trousseau. After the real attack, gastric symptoms, dizziness, colic, and cramps may continue for some days. The therapeutic measures here indicated are similar to those described in the article on Asiatic cholera.

The continued disturbances of the digestive functions, which sometimes occur towards the end of cholera nostras, will require the same careful attention as the similar conditions following Asiatic cholera.

The *bibliography* of cholera nostras will be found in conjunction with that of Asiatic cholera on page 441.

ASIATIC CHOLERA.

BY

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ASIATIC CHOLERA.

THE name cholera has for hundreds of years been the term used for a disease which begins with diarrhœa and vomiting, is followed by a severe clinical picture—marked weakness, cramps or spasmodic contractions of the muscles, cyanotic color of the skin, and great muscular weakness—and in individual cases leads to death. This disease appeared sometimes in single, sometimes in aggregated cases (small epidemics), particularly in summer and in autumn. Now, when in the year 1817 and the period following, the severe epidemic disease with similar symptoms but with a greater mortality which proceded from India, received the name of cholera, it became necessary to distinguish the two diseases from each other by a special term. Therefore, that of Europe without conveyance of the native Indian disease was designated cholera nostras (also C. Europæa or wrongly C. sporadica), whereas the Indian disease received the surname of its native land, India, or less specifically that of the entire continent, Asia.

History.

Cholera Indica or Asiatica receives its title from its native land, India. The original home, the endemic district of cholera, exists in the southern part of the province of Bengal in that low country through which the many-branched Ganges flows. The principal city of this district is Calcutta. In this territory the cholera remains mildly endemic practically all the year round, frequently so that its maximum appears in April, a favorable month for the disease on account of the heat and slight amount of rain, its minimum in the warm, wet August. This is not, however, the invariable rule.

According to the descriptions of Bryden this region possesses a constant warm, moist climate, caused both by the low situation as compared to the surrounding mountains and the enormous amounts of water which the Ganges and Brahmaputra from the northern and southern slopes of the Himalayas and from the mountainous regions between Assam and the valley of Irriwaddy, carry through in numerously branched streams. And this humidity of the soil is still further increased by the so-called monsoon, a southeastern rain-

bringing wind; as a result of these influences the annual rainfall averages seventy inches. It may also be of importance that even the period during which cholera rages, called in general the hot and dry season, is in no sense entirely free from rain. Whether, besides this region, other parts of India, such as the coasts of Malabar and Malwa as MacPherson seems to think, are to be designated as endemic cholera districts, is still an open question.

From the first-mentioned endemic territory, the cholera spreads practically year after year over the greater or lesser part of India and the surrounding countries of Asia, and thence has invaded Africa, Europe, and America in six epidemic marches. The thorough investigations of MacPherson have shown that the first Europeans who came to India, the Portuguese, found the cholera as an endemic, at times epidemic disease. It is said that as early as 1543 a great cholera epidemic was observed in Goa. Macnamara traces the origin of cholera to a still earlier date. According to him cholera was known long before the Christian era. The Indian Æsculapius Charaka (who, according to the belief of the Hindoos was taught directly by the god Dhanwantari) and his pupil, both of whom lived and worked in the northwestern provinces hundreds of years before Christ, undoubtedly described the course of cholera from the diarrhœa and vomiting of the beginning of the disease to the blueness of the lips and nails in the algid stage, and the vox cholerica. The disease was called vishūchikā or vishūhī (vomiting dysentery), also nirtiripa (intestinal colic), and according to some authors, mordechin (rapid death?). Nevertheless, within recent times, particularly on the part of R. Koch, a doubt has been raised as to the antiquity of cholera. Koch regards the reports of the older epidemics as very doubtful, and expresses it as his opinion that before 1817 genuine cholera was not endemic in any part of India. Basing his hopes on this belief he confidently thinks that, with energetic prophylactic measures in Madras, Calcutta, and Bombay, we shall be enabled to limit the cholera once more strictly to India, and then to cause its complete disappearance.

These views of Koch require us to undertake a new examination of the older accounts of the occurrence of cholera in India. In this respect the oldest Indian communications, of which Macnamara informs us, must first of all be verified. According to the courteous communications sent me by my former colleague, Prof. Justi of Marburg, the time of Suçruta as of the other numerous Indian authors is uncertain. Suçruta, who concluded the system of Indian medical science, probably lived between the sixth and eighth century of the Christian era. The Arabian Fihrist (a literary encyclopedia) informs

us that the work of Charaka, the predecessor of Suçruta, was transposed into Arabian from a Persian translation. The translation of these Indian works into the Persian took place principally under Chusran I. (531–578), and if Suçruta's work was in existence at that time, then they would have had recourse to this and not to the work of Charaka, which was superseded by that of Suçruta. The eighth century, however, is certainly the latest epoch at which Suçruta could have flourished, because his Yajurveda was translated into Arabian by an Indian doctor, during the time of Haroun-al-Rashid (786–809).

The description by Suçruta of the clinical picture of the so-called vishūchikā, for the translation of which I am indebted to Prof. Justi, is very suggestive of Indian cholera. After mentioning various disturbances such as diarrhœa, vomiting, thirst, darting pain, deafness, it further speaks of "the person, whose teeth, lips, and nails are blue, whose consciousness is slight, who is tormented with vomiting, whose eyes are sunken in their sockets, whose voice is weak, whose joints are all relaxed." However, inasmuch as in India sporadic cases of non-epidemic cholera also occur, a positive opinion, in the absence of more definite statements, in regard to the epidemic character of the disease is impossible. But we have further evidence. In the Vedas, which in part are older, in part of the same age as Suçruta's work, there is found a passage in which the vishūchikā is personified as it were and as the pest maiden is implored: "May the vishūchikā which, both tiger and wolf, does not touch the feathered falcon and the lion, protect these from terror and need." The offering of prayer for the turning away of a plague is familiar enough to us, but that such a prayer should be instituted as a protection against sporadic cases of cholera seems very improbable to me as well as to Professor Justi. Nevertheless I must not neglect to state that Albrecht Weber, the celebrated Sanscrit scholar, has expressed a different opinion concerning this passage. We possess, however, further strong evidence that endemic cholera existed before 1817 in Sonuerat's book of travels in East India and China. In this we find it stated that in a few years sixty thousand people died of a plague, the symptoms of which consisted in watery diarrhœa (often thirty movements in five to six hours) with vomiting, complete loss of strength, burning thirst, a feeling of anxiety, retention of urine, loss of voice, coldness of the hands and ears, and sinking of the eyeballs in their sockets. I know of no epidemic disease other than cholera which could be understood from this description. It appears, however, that after this great epidemic there was a period of rest.

The next accounts of the plague date only from 1817. After it had

appeared in Bengal in the year 1816, it arrived in Jessore in August, 1817. Looked upon at the beginning as the ordinary epidemic of that period of the year, it soon, on account of the great mortality, caused a panic of terror, and this increased still more when the disease spread from one community to another, from district to district, travelled over all Bengal, and also found no impediment in the mountains of Bundelcund and Rewah. At this period also the name cholera was given for the first time to this disease, which, as Inkes states, spread like the plague from the Ganges practically to the Indus, and from northern Bengal over the greater part of the Indian peninsula. Sydenham's report upon an epidemic observed by him in the years 1669, 1674, 1675, and 1676 and described under the name of cholera, was doubtless the cause of this designation. And, according to the Indian observations and the comparison with the descriptions of Sydenham, there seems to have been some ground for the identification of these two diseases. Diarrhœa, vomiting, anxiety, cramps of the legs and arms, coldness of the extremities, and fatal termination within twenty-four hours are the most important symptoms of the epidemic disease described by Sydenham. Still, this description might be applied rather to numerous cases of native dysentery, especially since painful evacuation and distention of the intestines are also mentioned among the symptoms. Perhaps, on the authority of Sydenham's book, the name cholera was used in India for sporadic cases and now was simply applied to the epidemic disease. The belief that the epidemic observed by Sydenham in 1676 was really one of cholera indica does not appear so very improbable from the description. Especially striking was the description of the cramps of the entire muscular system (Epistola I. Responsoria, p. 295), such as I have seen only in the clinical picture of Indian cholera.

After this appearance of cholera in 1816 and 1817 there occurred the first advance of the scourge outside of India. While the disease spread more and more in India, and by the year 1819 had reached a greater extent than at any time since, in the year 1818 Ceylon, and in the following two years Mauritius, Isle de France, and the east coast of Africa were attacked. At practically the same time Farther India was visited, and from here the plague spread over Sumatra, Java, and Borneo. In 1820 China was also invaded. In the year 1821 the disease was encountered in Arabia, on the coast of Persia, and in Mesopotamia. With the onset of cold weather the epidemic appeared to be extinct, but in the spring of 1822 it broke out anew in most of the affected districts. In 1823 Syria, Palestine, and the coast of the Caspian Sea were invaded, and on September 22d, 1823,

the disease for the first time entered upon European soil in Astrakhan, where it became extinct, however, in October.

The second epidemic of cholera began in the year 1826, with a wide spread of the disease along the Ganges and its adjoining rivers, as well as in the northwest provinces of India. From Lahore it reached, in 1827, by the caravan route, Cabul, Balkh, and Bokhara; in August, 1829, the province of Orenburg was invaded. At the same time Teheran was visited, from which the epidemic, after dying out in the winter, began to spread again in the spring of 1830 and once more reached Astrakhan. Now it travelled along the banks of the Volga, along the coast of the Caspian Sea to the mouth of the Ural River, and finally along the Caucasus range to the country of the Don Cossacks. Before the close of the year 1830 the epidemic had practically reached St. Petersburg, and even the cold winter of 1830–31 did not offer any barrier to its extension. In the spring of 1831 it appeared in the western provinces which until then had remained free, and in Poland where the military movements of the Polish-Russian war contributed essentially to its extension. In June the disease invaded St. Petersburg and practically at the same time Orel and Archangel, later also the Baltic Sea provinces. At the same time it was carried from Persia to Mesopotamia, Arabia, Palestine, and Egypt. From Russia the disease entered Germany. In June, 1831, the frontier town of Kalisch was attacked, and from here the disease spread over the provinces of Posen and Bromberg, entered the province of Silesia, and spread along the Oder to the River March and to Pomerania. Stettin, Frankfort-on-the-Oder, Cüstrin, Potsdam, Berlin, and later Hamburg were attacked. In the latter city the cholera remained until 1834. In 1835 and 1836 there were only a few fatal cases regarded by some as of cholera nostras, whereas in 1837 the southern part of the city, that is, along the banks of the Elbe, was once more visited by a small epidemic. In 1834 the disease was carried from Hamburg to Bremen. In addition to the land route cholera reached Danzig in May, 1831, from Russia, being carried most likely by Russian ships; Elberg, Königsberg, and the government district of Köslin were also attacked. Previous to this the epidemic had already spread from Podolia over the Galician border and thence reached Hungary, lower Austria, Moravia and upper Austria, further to the Moldau, to Wallachia and Turkey. Before the close of the year 1831 Great Britain was invaded, and in the spring of 1832 the cholera spread over great districts there. At the same time the disease appeared in Calais and Paris, and hence spread very widely through the lower departments of France. Belgium and Holland were also visited, and the disease was carried from

Rotterdam to the Rhine provinces, and found a favorable soil in Emmerich, Ruhrort, and Mühlheim, while in other places only isolated cases were observed. In 1834 the cholera extended widely in Norway and Sweden, not being limited to the coast, but spreading through the valleys of the interior. In the mean time, in June, 1836, the cholera had crossed the ocean, and had been carried to Canada by Irish immigrants, where it spread with enormous rapidity along the St. Lawrence and its tributary rivers, as well as along the shores of Lake Ontario. From here the United States were attacked. In August, 1832, the disease had already spread over a great district, and in 1833 it broke out anew, raged in the Indian territories and crossing the Rocky Mountains reached the Pacific coast. In the same year Mexico and the West Indies were visited. Of South America, only Guiana was attacked to a limited extent. In January of the same year cholera was brought to Portugal by an English ship, spread over Spain and thence reached Marseilles. From the latter place it entered upper Italy, and during this and the following year it spread over all of Italy, including Sicily. From upper Italy it reached the Tyrol, Dalmatia, and Illyria; from the Tyrol it entered Bavaria and attacked the city of Munich in addition to some places on the great routes of travel. Vienna, Galicia, Poland, and certain parts of eastern and northern Germany were also once more attacked. In all of these districts the epidemic reached only a mild extent, and by the spring of 1838 it was extinct in the regions outside of India.

The third advance of the cholera began in the years 1841 and 1842. After spreading to a great extent over India, it invaded China, the Philippines, and Persia and in 1844 reached Afghanistan and thence spread over Cabul, Herat, Samarkand and Bokhara; Mecca and Medina were infected by pilgrims and all of Arabia was invaded. In the spring of 1847 we find the cholera once more at the Caspian Sea and in Constantinople, whence a large part of Turkey, the countries of the Danube, Greece, and northern Africa were invaded. From Orenburg, Russia in Europe and Siberia were invaded. In 1847 Moscow, in 1848 St. Petersburg, and also the Baltic provinces and Poland were stricken.

From Poland, Silesia, eastern Austria, and large extents of northwestern and western Germany were infected. In Hamburg alone 3,687 cases of cholera with 1,765 deaths were recorded. In 1849 Great Britain, Holland, Belgium, and France were severely visited by cholera. Carried by emigrants cholera reached the United States as early as December, 1848, but did not become widespread until the following year. Mexico, Central America, and the Antilles were attacked. In 1850 Algiers, Tunis, Tripoli, and Morocco were visited; in 1852

various eastern provinces of Prussia; in 1853, during a very extensive epidemic, Denmark and the southern part of Sweden, in 1854 England, Scotland, Ireland, and France. In the same year the epidemic again reached the United States and Canada, and extended to the West Indies. In the fall of 1854 Bavaria and the southwestern part of Germany were visited. During the same and the following year, various parts of Switzerland, which in general had been thought immune, suffered from the disease. In 1855 cholera broke out in Brazil and spread over many parts of South America. The western coast of Africa was also attacked for the first time. Of great interest is the conveyance of cholera by a Sardinian bark to Fogo, one of the Cape Verde islands, upon which five per cent. of the population died. During the following years smaller outbreaks occurred here and there, as in Hamburg, in 1859, where 1,285 people died, but in the year 1860 cholera was extinct outside of India.

The fourth epidemic of cholera began with a severe endemic on the Ganges in the year 1863; in the same year Ceylon, China, and Japan were attacked; in 1865 the disease, carried from Arabia or the eastern coast of Africa, broke out among the pilgrims in Mecca. By the refugees, the cholera was carried in all directions. Egypt, Malta, somewhat later Gozo, Marseilles, Constantinople, Ancona, Valencia, and many other places were quickly attacked. From Marseilles the disease spread over the southern part of France; Italy, together with Sicily and Spain, were severely affected. From Egypt, Constantinople was infected in 1865 and thence the disease extended over the Balkan peninsula and the southern part of Russia.

In 1866 Moscow, St. Petersburg, Warsaw, and various cities of eastern Austria were visited. In 1865 there arose in Germany a very much discussed outbreak of cholera in Altenburg and the surrounding country, which was brought in by a family arriving from Odessa. In all 468 persons died. With this the epidemic became extinct. In 1866 there followed from Luxemburg an invasion of the cholera into the Rhine regions and Westphalia. Just after that cholera broke out in Pommerania and various Prussian provinces, in Hamburg, Saxony, Brunswick, Mecklenburg, Oldenburg, and Anhalt. Of 2,254 patients in Hamburg 1,158 died, in Prussia 114,683 people succumbed. In 1867 the cholera still held sway in the Rhine regions. At the same time it existed in Belgium, the Netherlands, and Great Britain, having been carried thither by a ship from Alexandria.

In 1865 the cholera also broke out in America and prevailed at various points until the year 1868. In 1869 and 1870, with the exception of Russia, the disease was extinct in all countries outside of India. Here it broke out anew in 1871, and in this and the follow-

ing year more than 200,000 lives were sacrificed. In the summer of 1871 it was carried to Prussia and then visited some eastern provinces, and later Berlin, Hamburg, Altona, Lüneberg, and Stade; yet the number of deaths was not very great, and in Hamburg for example reached only 141. In 1872 the disease was carried from Poland to Austria-Hungary. During 1872 and 1873 some 200,000 people succumbed. At the same time a small epidemic prevailed in eastern Germany until the year 1873, when, due apparently to a new importation, it appeared in a more severe form and raged again in an unexpected manner. During this year 1,729 cases of cholera with 1,005 deaths were reported by the Hamburg medical inspector; in Magdeburg almost two per cent. of the population was swept away. Altogether the number of deaths in Germany is said to have been 33,156. At the end of the year 1874 the epidemic was extinct in most places; only in Bavaria and eastern Austria a few cases developed in the spring of 1874. During the course of this epidemic (1873) the disease was once again carried to America; it appeared first in New Orleans and spread along the Mississippi and its tributary rivers. In 1875 the fourth cholera epidemic seemed to be extinct.

The fifth epidemic invasion followed a severe outbreak of the disease in Calcutta and Bombay in 1883. It spread to Japan, Egypt, and the coast of the Mediterranean, but did not reach a very great extent during this year. In the year 1884 it prevailed to the same extent in India, broke out in Toulon on June 14th, 1884, and from here spread over many departments of France and to Corsica, Algiers, and Italy. In Italy, Naples in particular was severely attacked. Of 10,000 patients, 6,000 died. In the above-mentioned countries the disease continued during the following years and in the year 1885 26,000 lives were lost in Italy. From 1885 until the beginning of 1886 Spain in particular was very severely visited. In all there were 338,685 cases, and 119,620 deaths. The provinces of Saragossa and Valencia were most severely affected. Almost at the same time 9,310 people died of cholera in Japan. The disease also existed in China and Farther India. In Japan it extended widely, in 1885, over large districts and caused 109,434 deaths. In June, 1886, Austria was infected from Italy. Then cholera broke out in Trieste, and here at the beginning of September reached its highest mortality. From Trieste the disease spread over all of Austria and Hungary. A very limited cholera epidemic, whose origin was not positively explained, broke out in September, 1886, in two districts situated near Mayence, namely, Gonsenheim and Fintpen. Fourteen people died here. The clinical diagnosis was corroborated by bacteriological examination. In Germany this appearance of the disease had no further consequence, and

a case imported into Breslau in November proved of no significance. A ship carried the cholera from Genoa to Buenos Ayres. From there it spread itself over various parts of Argentina and Chili. Beginning in the spring of 1886 a murderous epidemic prevailed in the East Indies. In 1887 the cholera still continued with severity in South America, particularly in Argentina and Chili. Also in various places of Austria, and in Italy, particularly in Sicily, fatal cases of cholera appeared. In 1888 Manila in the Philippine Islands and Farther India were visited. In Italy cholera occurred only in a few small places. In 1889 Europe appears to have escaped, while the epidemic continued in Japan, Farther India, and the Philippines. Cholera broke out in Bagdad on August 3d and continued to prevail in Mesopotamia until December. The number of deaths was estimated at 50,000. In 1890 cholera also appeared there and in Persia, though in a milder degree. In the same year China, Japan, Siberia were attacked by a mild epidemic, but in some Spanish provinces, especially in Valencia, 2,836 people were swept away. A few cases were carried into France and England, but the disease did not spread further. In the year 1891 cholera broke out in a very severe manner at a place of pilgrimage near Calcutta, and from here spread over India, Syria, Arabia, Siam, China, and Japan. In 1892 the disease was most severe in Calcutta. Crossing Afghanistan, the cholera entered Persia, destroyed many in this country and then spread along the Caspian Sea; in Russia, Baku, Astrakhan, and Nijni Novgorod were attacked. The disease advanced into the interior of the country along the railroads and water-courses, and in the first half of August a greater part of Russia could be said to be stricken. Up to November there were half a million cases with a mortality of over fifty per cent. While the cholera slowly advanced from the east towards Germany, suddenly in July, 1892, it broke out in Havre after Paris and its environment had already been suffering from a cholera-like disease since April. From Havre the cholera spread over the coast cities and into the interior. A sudden and quite unexpected outbreak occurred in Hamburg in the middle of August. After the occurrence of isolated cases in the harbor (partly in Hamburg, partly in Altona) on August 15th, 17th, and 18th, the number increased by the 21st and rose until August 27th, upon which day there were 1,024 cases. In the first days of September the number of cases decreased, still the epidemic lasted with a few cases until November 13th. In this space of time there was a total of 16,955 cases, with 8,605 deaths. Also in the following months until March 11th, 55 other cases of cholera were observed. The cities of Altona and Wansbeck, situated near Hamburg and practically forming part of it, but distinguished

at that time an account of the better quality of the drinking-water, were visited in but small numbers during the same space of time. Simultaneously with that of Hamburg a small epidemic prevailed in Galicia, Hungary, and other parts of Austria. From Hamburg the cholera was spread in all directions, especially over all of Germany, although a widespread epidemic did not occur; a few ship epidemics also followed. An interesting (and, as regards its origin, not fully explained) epidemic, broke out in the Saxony Insane Asylum of Nietleben in January, 1893, during which there were 109 cases with 52 deaths. In the mean time the disease prevailed to an unlimited extent in Arabia, Persia, Turkey, and especially in Russia. According to the official reports, there died in Russia alone during the year 1893 some 50,000 people. In other countries during this year only a few cases of cholera occurred, and these few led to no great epidemics. Bosnia, Hungary, France, Italy, and Spain, however, were visited. About 500 people died in Spain. In England, mostly in the seaports and their environments, a few cases also occurred. In Germany there appeared along the course of the Rhine 27 cases of cholera, mostly upon ships and in the harbors; from here in all likelihood the disease was carried to the neighborhood of Solingen. In Hamburg, 202 cases of cholera with 60 deaths were reported. Along the course of the Oder, Weichsel, and Memel cases of cholera were also observed, to a great extent among those engaged in work along the banks or who could have been infected by drinking the water. At the beginning of 1894, however, the German Empire was almost entirely free from the cholera, whereas in Russia the epidemic still continued to a slight degree. From Russia it appears to have gained an entrance into Galicia. In France, Belgium, and the Netherlands it was still present. Another unexplained conveyance of cholera took place in the Hessian village of Bürgeln. Furthermore the disease was carried from Russia to the already frequently visited district of Oppeln, as well as to West and East Prussia. The number of deaths, however, in contrast to the visitation of the neighboring parts of Russia across the frontier was very small. Towards the end of 1894 cholera appeared to be extinct in Germany, but in Turkey, Russia, and in the neighboring parts of Galicia cases still occurred epidemically. In these regions the disease also prevailed in 1895. It appeared also in Constantinople, and in April, 1895, among the pilgrims in Mecca. From here it was carried to Egypt. An extension towards the East also took place, and the Japanese troops at Formosa are said to have particularly suffered. In South America cases of cholera also occurred. Although Morocco was visited, the disease did not spread to other parts of the Mediterranean. Germany also

remained free despite the fact that in Russia the disease was not yet extinct. In 1896, the cholera became extinct in Russia and Austria, but appeared in Arabia and sacrificed a great number in Egypt. Besides this cases also occurred in the various Spanish islands.

Etiology.

With the attention which the Indian scourge, designated cholera, attracted upon its appearance in 1817 began the discussions as to the etiology of this disease. The medical authorities of Bombay declared that cholera prevails with equal frequency during all seasons of the year at temperatures above 4°–8° R. (41°–50° F.), during the months of long-continued, practically unceasing rain, as well as during the drought which hardly leaves behind a trace of vegetation; they also declared that it is carried from one place to the other, just as other contagions, and propagates itself like other recognized infectious diseases, citing many evident examples of this kind. Corbyn, however, was convinced that the disease is not contagious, basing his conclusions on the fact that he himself and all of his nurses inhaled, without any injurious effects, during all hours of the day and night, the air of the overcrowded cholera hospital. Contrary to the experience of Corbyn, Burrel reported that within the short space of six days practically every attendant in the hospital contracted the disease, whereas of the regiment of 800 men, living outside, only 100 were taken ill with cholera. David Graw, Whyte, Inken, and John Taylor adhere to the view of the contagious nature of cholera, but Wallace was unable to convince himself of the contagiousness of the disease. The same objections against the theory of the contagious character of cholera which have been raised in later times were urged at this also. The most important of these were that only a small percentage of the population were taken ill, and those chiefly who lived under unfavorable conditions, dressed poorly, and were badly nourished, or who were exposed to other numerous injurious conditions, such as cold or the use of indigestible and particularly raw food; that the disease spread along the routes of commerce and travel, especially in connection with the marches of troops; that it by no means, however, appeared in all places at the same time, and that it skipped some regions. A peculiar opinion was held by Thomas Whyte. He thought the spread of cholera depended upon unknown properties of the atmosphere, and above all laid the blame to the southwest wind as the conveyer of cholera. This opinion also found adherents at a later period, among these being Bryden, who, although he admits other modes of conveyance, incriminates, next to

the soil, the monsoon as the most important cause of the epidemic extension.

Von Pettenkofer deserves great credit for having undertaken a proof of these questions by a thorough epidemiological examination. As a result of this examination it was at first rendered doubtful whether human association was a factor in the spread of cholera and whether opinions such as those of Bryden ought to be rejected. Von Pettenkofer writes:

"The history of cholera at Malta appears to me to offer the most convincing proof that at any rate communication with infected places must precede the outbreak of a cholera epidemic, even though conditions of place, time, and person may be equally necessary for it."

The circumstances which could give a final answer to just this question were to be found more opportunely in the Maltese group of islands than perhaps in any other part of the world. The two islands, Malta and Gozo, have since 1837 been visited from time to time by cholera; both have the same character of soil and the same climate; both are equally susceptible to cholera as the course of all epidemics has shown. In the year 1865, for example, 12 out of every 1,000 in Malta and 16 out of every 1,000 in Gozo died; thus we can by no means say that Gozo has less susceptibility to cholera than Malta. Both islands are situated in the same sea, indeed separated but a short distance from each other, and have the same winds, the same rain and sunshine, the same population, the same manners and customs. It might certainly be held with all positiveness that all the conditions of place, time, and person, which in addition to the specific germs still belong to the cholera epidemics and from which cholera might arise autochthonously, were present upon both islands at one and the same time. They are distinguished solely by the fact that Gozo has no direct communication with the rest of the world, but only indirectly through Malta, the latter possessing excellent harbors, whereas Gozo does not have a single one. With the conformity of position, soil, climate, and all other conditions, with the exception of the communication, if cholera could rise autochthonously, if it could be carried by the air, or if for its origin communication with infected regions was not necessary, then it ought certainly to have appeared at the same time on both Malta and Gozo, or occasionally on Gozo somewhat earlier than on Malta. But this was never shown to be the case. The cholera invariably appeared in Gozo an appreciable time after it had broken out in Malta. In 1837, when the cholera visited the islands for the first time, the first case in Malta was on May 26th, in Gozo July 5th. In 1850, the first case in Malta occurred on June 9th, in Gozo on August

28th. In 1854 the first case of cholera in Gozo occurred on August 13th, long after the disease had shown itself in Malta. The first patient at that time came from Malta with the symptoms of cholera already developed, and it was not until August 19th that the first case occurred in a person who had not been in Malta. Likewise in the year 1856 the first case in Gozo was that of a person who came from Malta, already ill with cholera. In 1865 the first case in Malta occurred on June 20th, in Gozo on July 21st. Without exception, the cholera existed first in Malta, and not infrequently many weeks intervened between the occurrence of the first case at Malta and of that at Gozo, indeed a greater interval of time than between the outbreak of the disease in Alexandria and its appearance in Malta. In 1865 the first positive case occurred in Alexandria on June 2d, the first in Malta on June 20th. These and many other thoroughly well-authenticated investigations of von Pettenkofer point with certainty to the fact that it is human intercourse which causes the spread of cholera. True, the details of this extension are not always to be detected, but most of the individual channels through which the disease is distributed are so evident that there can be no doubt as to this mode of extension. "The cholera has never advanced," says Griesinger, "like a broad stream inundating entire countries at one time, bringing disease to all regions lying parallel with each other, over a wide extent, but always advances in relatively narrow lines from which usually, but not always, lateral offshoots arise. In countries with a small population we see constantly that this district corresponds to the great lines of travel. If the disease overstep high mountains, if it pass through a desert, if it cross the ocean, it always follows the paths of human intercourse, the post and military routes, the caravan and sailing routes, etc. If it has broken out on an island, then the first cases have always been in a seaport, never in the interior. In all somewhat more densely populated regions, with rapid means of communication, the cholera does not advance continuously and regularly, but rather irregularly and by leaps, so that frequently large tracts of land situated in the centre remain free, are overstepped as it were. For example, in 1848 the cholera had advanced in Russia only as far as Moscow and Smolensk, when it suddenly broke out in Berlin, all the intermediate district having been spared."

Equally interesting as this case cited by Griesinger is the leap which the cholera in 1865 made from Odessa to Altenberg, where a woman who had arrived from Odessa took sick and died in the house of her sister-in-law two days after her arrival. On the day of her death the sister-in-law was taken ill and died the following day, and then an epidemic followed, which with a few short intervals continued into De-

cember, and with a slight extension to a few neighboring cities was attended by a mortality of 468. A no less interesting case of the conveyance of cholera is reported by Virchow. In Virchow's ward in the Charité, situated up three flights and shut off from the rest of the hospital, there was admitted on September 17th, 1871, at five o'clock, P.M., a vagrant in whom eight days previously vomiting and diarrhœa had been observed. The clinical picture corresponded to typhoid fever. The patient died on September 20th. The patient was nursed by three of the attendants. Of these, one, a man sixty years of age, with ulcer of the legs and œdema of the feet, was taken sick with cholera on September 21st and died in a few days; the second was also very sick with the disease, but recovered in the cholera hospital which had been erected in the mean time, and the third was taken ill with a diarrhœa of eight days' duration. Virchow emphasizes the fact that the first patient, after his old clothes had been taken off, received a bath and then at once fresh clothes, so that as far as his body was concerned he was an entirely new person, so to speak. Of interest also is the conveyance of cholera by the Hamburg military contingent in the year 1866. A few days before the departure of the troops, the cholera broke out in Hamburg. In the garrison, a case occurred on July 20th which ended fatally in a few hours. On July 22d the troops went directly to Aschaffenburg. From July 24th to August 6th, that is, within nine days, 13 of the 1,695 men died with cholera. During this and the following period the troops were distributed over forty different localities. Here, however, a peculiarity of cholera showed itself, of which we shall speak later on. Cholera epidemics broke out in but four of these places, sporadic cases occurred in thirteen, and twenty-three remained perfectly free. The other small epidemics which were caused in Franconia and Baden by the Prussian troops also showed the same limitation to a circumscribed and well-defined territory.

In the last German epidemic there were also some characteristic cases of cholera conveyance which may be mentioned. Of particular interest are those cases in which the disease was spread by articles of food (Kossel, Steyerthal). It should be noted, however, that a great deal of mischief may be caused by the attempt to trace an outbreak of cholera to special individuals. In many of the cases of cholera conveyance cited in literature, the germ of disease, as Pettenkofer states, may have been brought in long before the outbreak of the epidemic, and thus the appearance of cholera and the arrival of a cholera patient may be simply a coincidence. This is all the more possible since not only true cases of cholera, but also cases of choleraic diarrhœa have the power to spread the disease. Moreover,

we know that cholera may be conveyed by apparently healthy people who come from a region in which an epidemic prevails or from an infected district. Such observations have been noted by Wachsmuth, Ackermann, Köstlin, and others. The first mentions the conveyance of cholera from Gieboldehausen into the surgical division of the hospital at Göttingen. As spreaders of the disease none but the physicians could be blamed, but of these none was taken sick. Ackermann, in his studies upon the cholera epidemic in Mecklenberg, found that the outbreak of cholera in Bützow, Stavenhagen, Schwerin, Güstrow, and two estates in the neighborhood of Güstrow, could be explained only by the carrying of the disease by healthy individuals. Furthermore, Köstlin has told us of a typical case of the conveyance of cholera from Stuttgart to the neighboring town of Hesslach by a healthy woman. First, her husband, forty-two years of age, was taken sick and died in two days, and after that a son, who recovered. The idea that the conveyance could possibly have been caused by infected wash must be rejected in this instance.

Alongside of these examples, however, there is no lack of others in which, despite immediate association with cholera patients, the anticipated transmission of the disease did not occur. Thus Günther reported the following on the occasion of the second Berlin cholera conference: In the epidemic of 1873 in Saxony during which 365 cases of death occurred in 52 places, not one of the 50 practising physicians died, and only 3 were lightly ill. In the year 1866 during our greatest epidemic, where in the district of Zwickau alone 2,638 deaths occurred in 118 places, of the 150 physicians who were treating the cholera patients not one died.

James Cunningham, in a year during which the cholera in India was widely epidemic, collected statistics concerning the number of orderlies in 67 garrison hospitals within the epidemic territory. Among the 67 hospitals of which each one admitted cholera patients, although in varying numbers, in only 8 did any of the attendants suffer from an attack of the disease, the total number of cases being 22. In the remaining 59 hospitals not a single case occurred among the attendants. In Dharmsala alone could it be said that many of the nurses were affected; here 8 nurses, 2 chair carriers, and 1 hospital officer were taken sick. Bauer, in his report of the Munich hospital "links der Isar" says: "A very important fact for the whole question of infection appears to me to be given by the condition of the attendants; thus of the nurses among the Sisters of Mercy only four, and one female servant were taken ill. The first took sick on August 19th, the second and third a few days later (summer epidemic), the fourth and fifth in January 22, 1874 (winter epidemic). Cholera pa-

tients had been admitted to hospital from without since June 25th, 1873, and before the first nurse was taken ill more than one hundred cases of cholera had already been under treatment; and strange to relate, the first infection which had evidently had its origin in the hospital occurred, not in a female attendant in the cholera division, but in one in wards Ten to Fourteen, where other patients lay, but where, on August 15th, house infection appeared, so that Sister Malachia could have been taken ill on August 19th by means of ectogenous infection just in the same manner as a phthisical patient, who was in the hospital for fully two months, was taken ill on August 15th. Remarkable also is the similarity of the cases on the one hand, and on the other the great interval between the first three and the last two cases of illness among the attendants. The latter could not be explained by contagion, inasmuch as cholera patients were continually present and their nursing was continued in exactly the same manner.

During the great cholera epidemic of 1892 in Hamburg, seven of the old and newly appointed attendants of the New General Hospital were taken ill, and three of these died. There was, consequently, a mortality of one per cent. among three hundred attendants. In the old General Hospital, besides the director and two physicians, thirteen of the old and newly appointed attendants were taken ill. Of these four died. But as one of these had not passed the last few days before his illness in the hospital the number of deaths must be reduced to three; among three hundred attendants this also gives a mortality of one per cent. Higher than this it cannot be reckoned under any circumstances, inasmuch as at times over six hundred persons were engaged in nursing cholera patients in the hospitals. This mortality is less than the general mortality, which gives 13.44 deaths for every thousand inhabitants. Nevertheless the vigorous age of twenty-five which was possessed by the majority of our attendants shows, according to the classification of Reincke in contradistinction to the previous admissions in the Hamburg epidemic, fewer cases of cholera and fewer deaths than the ages between one and five and fifty and seventy, so that the small number of our attendants corresponds pretty well with the total mortality. If we consider that by this number some eight thousand cholera patients were nursed, then this experience does not in any manner substantiate the theory of the transmission of cholera by direct contagion.

The experience of the smaller epidemic in 1893 was somewhat different. During that epidemic, from September to November, 82 cases of severe cholera and 69 cases of cholerine or choleraic diarrhœa were treated in the New General Hospital at Hamburg. Of this

number 42 died. Twenty-six persons were engaged in nursing these cholera patients, two attendants assisted in the examination of the dejecta and cultures. During this time a potato peeler, two male nurses, one female nurse, and the attendant in the anatomical department who assisted in examining the stools, took sick with cholera or choleraic diarrhœa. Of the attendants, only those were taken sick who were occupied in nursing the cholera patients; the rest of them remained perfectly well. Of those who took ill and in whom the diagnosis was confirmed by bacteriological examination, not one died; three were entirely capable of working during the short illness, while one was at times very sick. This experience is apparently contradictory of that of the epidemic of 1892, but only apparently, as I believe. Were we to count only the fatal cases, then indeed we should be apt to draw the false conclusion that during the cholera epidemic of 1893 no infection of the attendants took place, whereas as a matter of fact they were attacked in surprisingly large numbers, but the mortality was *nil.* This fact could be demonstrated, however, only by a careful bacteriological examination. That the disease was of a mild form was in accord perhaps with the known fact of the greater resistance of youth, which is evident from the above-mentioned conclusion of Reincke founded upon a study of the Hamburg epidemic and from the results of my own experiences. Of particular interest was the illness of the attendant in the anatomical department who assisted in the examination of the dejecta and cultures, and that of a servant in the Hygienic Institute of Hamburg who was occupied in a similar way. The results of the most thorough studies of various observers point to the evacuations of patients with cholera, as well as of those with choleraic diarrhœa, as the carriers of the contagium. The stools themselves are not always specifically mentioned, but in many cases the clothing soiled with the dejecta of cholera patients apparently conveyed the disease to the washerwomen. In certain cases the soiled linen of a cholera patient was found to have been the cause of an epidemic outbreak in a new locality. In all these cases, however, the intestinal discharges conveyed by the clothing were looked upon as the real cause. Von Pettenkofer, however, is more cautious in accepting such conclusions; indeed, he looks upon soiled linen and clothing as the spreaders of cholera, but with respect to the nature of their adherent infectious matters he warns us against hypotheses, especially as some very competent observers were unable to find anything abnormal in the dejecta of cholera patients.

Predisposing Causes.

Local Conditions.

According to von Pettenkofer, in addition to the unknown something which gives rise to cholera epidemics through human association, there is still necessary a special regional and seasonal disposition in order to make possible a spread of cholera. The size of the epidemic, that is to say, the number of patients, depends upon the individual disposition of the population. Therefore von Pettenkofer does not consider cholera as a contagious disease in the sense that the infectious matter grows only in the human body. If from this point of view we compare cholera with another epidemic disease, influenza, then indeed some very essential points of difference become evident. Whereas influenza spreads over wide regions in a more or less coherent advance, and attacks for the most part simultaneously and uniformly a large percentage of the population, without skipping individual districts or sparing or attacking more severely certain favorably situated regions, we see in cholera, for the most part, a characteristic local development, rarely a uniform extension over an entire city. Cholera spreads in all directions from the primary, secondary, or tertiary foci, but not uniformly, halting sometimes here, sometimes there, and by manifold conveyances forming new foci of infection at widely separated points, which may eventually far surpass the primary ones in size and extent. In this radiation from the primary focus we see, however, individual regions, which are no more isolated from the rest of the world than these, remain perfectly free for a long time despite the fact that the conditions of the cholera conveyance appear to be the very same. In reference to this I refer to the work of von Pettenkofer relative to the cities of Hamburg and Berlin which, despite constant intercommunication, have seldom suffered simultaneously and equally from cholera. In the history of cholera, moreover, similar examples are by no means wanting. Furthermore we know that typical cases of cholera have occurred frequently in isolated regions without giving rise to epidemics in such places. In the numerous instances of cholera conveyance which took place from Hamburg in 1892, the most varied means of precaution against the spread of the disease were enforced; but similar observations have been made in former times in which the disease acted in the same way, although no such preventive measures were employed. It happened many times that those cases remained isolated, and were followed by no epidemic, indeed, by no other case of cholera. A very typical instance of this kind is related by von Pettenkofer. On

December 7th, 1873, there was discharged from the jail at Lauffen, in which at the time a small cholera epidemic prevailed, a prisoner who concealed the fact that he was suffering from diarrhœa. Up to the evening of the following day he tramped through several villages, suffering all the time from a diarrhœa with numerous colorless movements and occasionally from vomiting; on that evening he passed several hours in the stage coach, coming in contact here with a large number of people who were on their way to a place of pilgrimage. On this same evening he reached Vilsbiburg, and only with exertion could he drag himself to the hospital, where he collapsed in a condition of cholera-typhoid, but eventually recovered. Despite the fact that his clothes were thoroughly saturated with fæces, and all along the route which he had traversed he evacuated abundant, apparently typical cholera stools, no cases of the disease followed.

A case similar to this in some respects was observed in 1893 by Dr. Schmalfuss, and was communicated to me by Dr. Reincke. During the cholera epidemic of 1893 a tradesman was taken sick on September 29th with vomiting and thin stools; he did not attach any importance to this fact, however, and started on his vacation, as he had planned a long time before, travelling directly to Thale, where he lodged in a hotel. During the next few days he felt quite well, walked about eight hours daily, but had very little appetite, and passed daily one or two soft stools. On the morning of the 25th he felt more miserable, and vomited once in the water-closet of the hotel. At 9:15 he left Thale, changed at Magdeburg, and travelled by way of Stendal to Hamburg, where he arrived about 5:45. In the railroad car he retched a number of times, and expectorated a small amount of tenacious mucus. He expectorated either into his handkerchief or upon paper. The toilet-room next to the coupé he used but once on the way from Magdeburg to Stendal. From the railroad station he was taken to a physician's office in a carriage. During the night he was taken severely sick in his home with a cholera attack, with vomiting, profuse diarrhœa, vox cholerica, and anuria. The diagnosis was confirmed by a bacteriological examination. This patient, it is true, did not make such extensive migrations as that described by von Pettenkofer; but despite the fact that he, beyond any question, carried the cholera from Hamburg, he did not in the course of his travels give rise to any infection, as far as could be learned. Cases similar to these have been noted in other places, such as Salzburg, Frankfort-on-the-Main, and Lyons, in which the individual with cholera, despite frequent opportunity for the development of epidemics, was never the cause of such, although he may have transmitted the contagium to other individuals.

We must not forget, however, that certain regions and districts were for a long time considered immune against cholera, until a later epidemic showed that this view was based upon an error. Würtemberg and Switzerland, both of which seemed time and time again to be immune, had their epidemics in regular order.

In strong contrast with the continuous and remarkable protection from cholera of certain regions stands the fact that other localities, whether cities, villages, or only certain parts of a city, were frequently attacked by cholera and also were sharply distinguished from other cities, villages, or districts by very high morbidity and mortality figures. The number of these observations is so great that it would be superfluous to mention the individual details. The regions which seem particularly predisposed for the outbreak of cholera are especially low-lying and damp regions, and particularly such as are conspicuous for their unfavorable sanitary conditions. Similarly we find occasionally certain countries or provinces which are especially prone to invasion by cholera. The province of Silesia, as regards the prevalence of cholera, is perhaps not the worst of all the Prussian provinces, but Oppeln is certainly the worse district in that province. Pistor has shown that Oppeln suffered from twelve epidemics during the period from 1836 to 1874, during which time Bavaria had four and Saxony six epidemics, and that in the district of Oppeln with an average population of 1,025,728, in the course of twelve epidemics there were 21,330 cholera deaths, or during each epidemic year 17.25 out of every 10,000 inhabitants; whereas during this time in all of Bavaria there were but 12,059 deaths, and in all of Saxony only 9,713 (7.30 and 6.52 per 10,000 respectively). But even within the limits of certain districts, some regions always show a peculiar predisposition to cholera, whereas others remain entirely free or suffer but slightly in each epidemic. These regions, designated as cholera-immune, are distinguished advantageously, as Förster showed in a very thorough examination, by the character of their water-supply from the regions which are severely visited by cholera. Some of these, as the much spoken-of cholera-immune railroad centre of Lissa, have a good aqueduct protected against contamination; some, as Jauer, deep wells fed by water from under a layer of rock thirty to forty feet thick; others, as Schmiegel, are supplied by water filtering through a deep layer of lime and clay, and thus are protected from sewer or privy contamination.

A most remarkable and frequent prevalence of cholera is shown in regions and districts situated on rivers and canals. We might attribute this tendency to cholera visitation to the fact that the rivers and canals are among the main routes of human intercourse, and so

cholera is disseminated. Still cholera has prevailed extensively in regions whose rivers and water-courses are not navigable.

Another explanation of this susceptibility is offered in the greater dampness of the soil and its consequent insanitary condition. Von Pettenkofer, as a result of very extensive investigations, has ingeniously sought to explain this local predisposition to cholera in different cities by the varying condition of porousness, of dampness, and of contamination of the soil. Nevertheless the differences between the so-called cholera-immune regions and those which have suffered frequently from epidemics, are by no means so characteristic and uniform that upon these differences alone the doctrine of local disposition to cholera could be established. Even the canalization which von Pettenkofer used in support of his theory cannot be of any great significance as regards cholera immunity when we consider that the city of Frankfort, which only began the construction of the Schwemm canal in 1867, might be designated as entirely immune from cholera, whereas Hamburg, which for very many years possessed a model system of canals, had such an extensive epidemic in 1892. Von Pettenkofer, after demonstrating repeatedly the influence of the rivers flowing through valleys and the dampness of the soil, alleged the height of the ground water as the best index of the changing conditions of moisture in those porous layers lying above the level of this ground water, and compared these variations in the ground water with the curve of the cholera cases. In certain places a uniformity appeared to exist in so far that the cholera morbidity varied according to the depth of the ground water. In other places, however, a relation between the two could not be demonstrated, and to overcome this difficulty von Pettenkofer, in addition to the condition of the ground water, also takes account of the rainfall. In Germany, the maximum of cholera morbidity frequently coincides with a low level of the ground water. It must be remembered in this connection, however, that this lower level as a rule occurs during the middle and latter part of the summer, during which time climatic conditions also favor the extension of cholera. The decrease in the number of cases of cholera and the diminished disposition of the epidemic to spread after a heavy rainfall, might be explained by the fact that as a rule rains coincide with a cooling of the atmosphere.

Further it is not unessential to the discussion of this question to remember that the coincidence between a high level of the ground water or abundant rain and a decline in the prevalence of cholera seems to be most evident in regions in which the water-supply is directly influenced by both the amount of rain and the varying level of the ground water. In certain cases in which the drinking-water is

derived from the superficial or deeper layers of the soil, we can readily understand that with the sinking of the ground water contamination of the soil by cesspools and the like would result in a fouling of the springs and ponds; moderate amounts of rain often act in the same way, whereas with more copious rains a thorough penetration and cleansing of the soil as well as of the water-courses takes place. The previously mentioned examination by Förster of the water-supply of various regions in Silesia and Posen bears out this assumption.

Even though we might find a satisfactory explanation of the prevalence of cholera in these facts, nevertheless it would hardly be advisable to attribute the regional disposition only to the condition of the ground water and to the amount of rain. It would be far more rational, in place of the soil alone, to take into account also the habitations with all their appurtenances, especially since the occurrence of winter epidemics, which run their course during a time of frozen soil, of ice, and snow, can thus be explained without difficulty. It goes without saying that to the question of habitations belong also those of the method of removing fecal matters, the water-supply and its relation to the privies and drain pipes, the nature of the foundations, as well as that of the position of the house, with reference to light, shade, and moisture. Furthermore, we ought to have details as to the various parts, the rooms and apartments in each house, although such details can with difficulty be represented with sufficient clearness to be of service in our investigations.

More than that, we must remember that there is by no means a connection between the occurrence of a case of cholera and the condition of the sufferer's dwelling apartments. Particularly in the large cities the dwellings serve but a short space of time as the places of abode for the men, who, as Koch and Flügge well say, may very easily indeed acquire a disease in their places of employment and in the neighboring cafés. If cholera is thus introduced into any particular dwelling, and then other members of the family acquire the disease, it will be incorrect to invoke the local conditions in explanation of the outbreak. On the other hand, however, a laborer may contract cholera in his home, while the disease actually breaks out at his place of employment, as a result of some special exciting cause, such, for instance, as drinking when the body is overheated.

Such considerations warn us that the epidemic facts also must be used with caution as a basis for theorizing, and that positive conclusions can be established only upon repeated and uniformly recurring observations. To these uniformly recurring facts belongs the following, however, namely, that the cholera prefers to such a great extent certain cities and certain parts of the city, that it fre-

quently occurs in the same quarter during repeated epidemics and remains here for the greatest length of time. The reason for this phenomenon may be a double one. In the first place these quarters may be especially exposed to the means by which the disease is carried (which is certainly a factor of importance in many cases), or secondly, the cholera germs may have been sown broadcast, so to speak, over an entire region, but find only in certain houses a favorable soil for their development. In these houses, therefore, cholera spreads most quickly and severely and persists the longest.

Let us see then what are the particular qualities upon which depends this special susceptibility of certain places and quarters. That a low-lying situation and unfavorable sanitary conditions must be regarded as etiological factors, to a certain extent at least, has already been said. It would be well, however, to study somewhat more in detail the individual points which enter into this causal complex. During the Hamburg epidemic of 1892 the parts of the city known as Harvestehude and Rotherbaum were attacked least severely, whereas Altstadt-Nordertheil, Neustadt-Südertheil, and Billwärder-Ausschlag were most severely affected.

Among every thousand inhabitants there occurred in

	Cholera cases.	Deaths.
Harvestehude	10.11	4.48
Rotherbaum	11.33	5.91
Altstadt-Nordertheil	34.17	17.52
Neustadt-Südertheil	39.58	19.91
Billwärder-Ausschlag	40.13	24.16

If we compare these districts we note that in the first two the houses are isolated for the most part and surrounded by gardens, in the latter they are all tenement houses with apartments looking on to courtyards. Whereas in Rotherbaum and Harvestehude each inhabitant has a floor space of from 90 to 180 square metres (970 to 1940 square feet), in the other three districts we may reckon perhaps 16 or at the utmost 30 square meters (170 to 320 square feet) to the individual.

A similar picture is also given by the comparison of cholera cases and deaths occurring in classes of the community divided according to the yearly income. A study of the following table shows us that it is the classes with an income under 600 and from 800 to 1,000, and from 1,000 to 2,000 marks which furnish an extraordinarily large contingent of the cholera cases. Those with an income under 600 marks, as well as those with an income of from 800 to 1,000 marks, were the greatest sufferers. This includes the greatest number of married and unmarried unskilled laborers, whereas in the

first group, with an income of 600 to 800 marks, belong many of the domestics of the wealthy families. These statistics seem to corroborate the old idea that cholera is preeminently a disease of the least

Classes arranged according to their income.	Taxpayers in the year 1871.	Total number of cholera		Among every 1,000 inhabitants there occurred	
		Cases.*	Deaths.*	Cases.	Deaths.
Over 600 to 800 marks.....	47,447	1,575	873	36.25	20.09
" 800 to 1,000 "	28,647	3,264	1,772	113.94	61.86
" 1,000 to 2,000 "	43,844	4,396	2,425	100.25	55.30
" 2,000 to 3,500 "	14,544	685	389	47.10	26.75
" 3,500 to 5,000 "	6,125	243	135	39.69	22.04
" 5,000 to 10,000 "	5,649	175	88	30.98	15.58
" 10,000 to 25,000 "	3,328	60	32	18.03	9.62
" 25,000 to 50,000 "	1,182	20	13	16.92	11.00
" 50,000 "	834	5	4	6.00	4.80
Total.....	147,604	10,423†	5,731†	70.61	38.83

favorably situated classes of the population, and that it reaps its richest harvest in the proletariat of large cities. It needs no argument to prove that conditions most favorable to the diffusion of cholera germs must exist in cramped tenement houses, with the frequently small and dirty kitchens which serve at one and the same time for wash- and dining-rooms, with the common and often insufficiently isolated privies and their drains, and with the close association of the children with one another.

We may say also that there is a special predisposition of certain callings, apart from the above-mentioned moments, for it has been shown that laborers without any fixed calling, who sought work at the harbor, especially those who worked or lived on the water, suffered most from cholera. This fact is rather remarkable in that the river population does not belong to the class of the hygienically unfavorably situated. During the greater part of the day they live in the open air engaged in healthy physical work and for the most part receive wages enough to be able to procure for themselves a sufficiency of nourishing food. And still we see that the cholera prevails among them during the summer, which is the very season when their mode of living is apparently the most hygienic. That the raftsmen of the Weichsel and Oder are frequently the first to fall victims to cholera, that they often contribute to the spread of the epidemic, and

* The women and children who did not pay any taxes, and who were taken sick or died with cholera, are reckoned in the class of those who supported them.

† Of those who were taken sick or died, 3,347 and 1,648 respectively had an income under 600 marks, whereas the income of 3,168 and 1,226 respectively was unknown.

that the river banks where the greatest confluence of raftsmen and sailors occurs become veritable plague spots during a cholera season has been known for a long time. A short time ago Reincke, in a work treating of the cholera epidemics of Hamburg in their relation to the water, showed that in all the epidemics the morbidity was much greater among the shipping than in any part of the city. We might say for all practical purposes that the river population was twice as severely affected as that of the next most unfavorable portions of the city, although it is probable that in the course of a long epidemic the river population varies greatly from time to time, so that as a matter of fact more people were exposed to the danger of the disease in the harbor than a census taken on any definite day would show. On the other hand we must take into special account the fact that small children, the aged, and chronic invalids, who on land contribute so largely to the cholera cases, are found in relatively small number among the river people. Neither the soil nor the ground water can be considered as active in the etiology of these cases, but the most important factor in the etiology of cholera is on the other hand most active. This is that the sailors and dock laborers derive their water-supply in great part from the same place into which the fecal discharges of the entire river population are deposited. To what a great extent the river population of the Elbe was involved in the cholera of 1892 is shown by a classification of Reincke, in which the count from December 1st, 1890, is set down as the foundation for the total number. That this was essentially much greater than during the cholera period of 1892 cannot be assumed.

River population on December 1, 1890.			Took sick.	Died.	Of every 1,000 there occurred	
					Sick cases.	Deaths.
Over 15 years	Males	8,947	291	115	73.3	29.1
	Females	322	54	28	167.7	87.0
Under 15 years		263	42	28	159.7	106.5
Total		4,532	387	171	85.4	37.7

These statistics show a cholera mortality much greater than that in any other of the most severely affected parts of the city. The seagoing ships appeared to suffer far less from cholera than the river craft. Inasmuch as in these, every influence of the land is abolished with the departure from the harbor, so von Pettenkofer must have considered these as immune regions in conformity with his theory.

Some examples which von Pettenkofer presents serve to corroborate this idea, and it cannot be denied after these observations that ships do not appear to afford a particularly favorable soil for the development of cholera. Nevertheless further observations have shown that von Pettenkofer's views upon the immunity of those on sea-going ships was not altogether correct. Of the older observations I will only mention the report by Virchow, at the cholera conference of Berlin, concerning the epidemic of 1885 on the *Franklin*, and at the same time the discussion by Robert Koch of the epidemics on the *Matteo-Bruzzi*, the *Acomac*, and the *Crocodile*. Of von Pettenkofer's own observations we need only mention those of the frigate *Apollo*. Relative to these ship epidemics, von Pettenkofer appeals to his formerly expressed opinion that according to experience the infectious cholera matter is but rarely carried from the land to a ship; but that in exceptional cases it is carried to such an extent that just as severe epidemics occur on the ships as on land. What this depends upon is a question which requires a more thorough examination, and everything taken on ship from the harbor must be subjected to a very searching investigation. An enormous amount of infectious matter must have been taken from Hamburg to the ships, but especially worthy of note is that most of the ocean steamers which left the harbor of Hamburg previous to the cholera epidemic of 1892 drew their entire water-supply from the Elbe. Thus, on the ship *Francisca*, which left Hamburg on October 13th, 1855, with 220 cabin passengers and reached Rio de Janeiro on December 12th, 53 persons were taken sick with cholera and 16 died. In 1866 there sailed from Hamburg to New York the following ships with cholera cases on board: On August 15th the steamship *Bavaria* with 278 passengers and 6 deaths; on November 7th the sailing-vessel *John Bertram* with 455 passengers and 36 deaths; on November 12th the sailing-vessel *Washington* with 207 passengers and 19 deaths; on November 28th the sailing-vessel *Jessie* with 241 passengers and 16 deaths. In 1867 the sailing-vessel *Lord Brougham*, which left Hamburg with 383 passengers, had 78 deaths from cholera among passengers and crew; the sailing-vessel *Leibnitz*, 543 passengers and 107 cholera deaths. Also in the year 1892, a large number of cholera deaths occurred on many ships which left the harbor of Hamburg at the end of August and the beginning of September. Recently Pfuhl has studied the reports of cholera epidemics upon the Italian emigrant ships in the year 1893, and as a result of this has come to the conclusion, contrary to that of Pettenkofer, that severe epidemics are the rule on shipboard. On the four ships, *Carlo R.*, *Andrea*, *Doria*, and *Remo*, which had a total of 4,466 persons on board, 311 died from cholera, that is, 7 per

cent., a proportion of the total population such as even the recent Hamburg epidemic does not show.

From this it follows that very severe cholera epidemics occur on ocean vessels, and that these may be much more serious than the epidemics on land. This is all the more remarkable, since the number of children, old people, and invalids on these ships was much smaller in proportion to the total population than prevails on land. Then Pfuhl examined further how the cholera germ reached the affected ships, and came to the conclusion that there was no infection in the freight, and especially that the water taken on at Genoa was clean. It seemed most probable that the disease had been carried aboard by emigrants who had become infected in Naples previous to embarking. A very remarkable instance is that cited by von Pettenkofer, according to which upon the ship *Renown* the cholera is said to have broken out, remote from Gibraltar, the last port of call, upon the same day on which cholera appeared epidemically in the harbor which the ship had left fourteen days before. This was certainly an extraordinary case, in which an explanation by means of personal contagion is absolutely untenable, and the only means we have of solving the riddle is by studying other reports of ship epidemics, especially the more recent ones.

Among the ships which left the harbor of Hamburg shortly before the epidemic there was the *Rugia*, which left the harbor on the morning of August 21st. On the following day, that is, on the 22d, a mild case of cholera occurred, which ran a favorable course in the hospital. On the 23d, 24th, 25th, 26th, 27th, 28th, and 29th of August nothing occurred. On September 1st two cases of cholera suddenly appeared, of which one ended fatally; on September 2d nothing; on September 3d ten cases of cholera with three deaths; on September 4th, three cholera cases with one death, and during the following days until September 9th, five, four, one, three, one cases of cholera with recovery. This observation strengthens our belief that the course of cholera observed on the *Renown* was not due merely to chance. On the *Rugia* the actual outbreak of the epidemic, as compared with the course of events on land, appears to have been retarded. We reach the same conclusion from a study of the following table, in which are recorded the deaths which occurred on the ships of the Hamburg-American line; from this list we except the *Moravia*, upon which almost exclusively children were attacked, on account of a doubt as to the nature of the disease.

August 22, 23, 24, 25, 26, 27, 28, 29, 30, 31	September 1, 2, 3, 4, 6, 7, 8, 9, 10, 11
0, 0, 0, 0, 0, 0, 0, 4, 8, 1	4, 7, 8, 5, 1, 2, 0, 1, 0, 1

According to this table we see that the epidemic takes the same course on sea as on land. In this case we should certainly be justified in assuming that the cholera was not conveyed from person to person, but that it was caused by infected drinking-water. Occasionally it has also been observed upon ships that high temperature of the air seemed to favor an outbreak or a greater extension of cholera, and here we touch upon a further accessory cause of cholera, the season of the year.

Seasonal Conditions.

Whereas cholera prevails in India all the year round, an incursion into the temperate zones takes place, as a rule, only in the warm season of the year. Summer and autumn are in central Europe and especially in Germany the times during which cholera prevails epidemically. With the beginning of winter the extension tends to cease, and often enough the epidemics disappear altogether. The same applies to America. In reference to this the following statistics concerning cholera morbidity and mortality in the Prussian Empire from 1848 to 1859 are of particular interest.

Period.	Cases.	Deaths.	Percentage of mortality.
From 1st to 15th April	71	50	1.0
" 16th to 30th "	110	62	1.2
" 1st to 15th May	192	112	2.2
" 16th to 31st "	650	334	6.7
" 1st to 15th June	3,819	1,961	39.2
" 16th to 30th "	4,894	2,431	48.9
" 1st to 15th July	6,106	3,050	61.0
" 16th to 31st "	10,866	5,430	108.6
" 1st to 15th August	21,870	11,674	233.4
" 15th to 31st "	41,758	21,966	439.2
" 1st to 15th September	57,395	31,048	620.9
" 16th to 30th "	45,415	25,518	510.2
" 1st to 15th October	35,874	19,462	389.2
" 16th to 31st "	29,903	15,809	316.1
" 1st to 15th November	21,215	11,363	227.2
" 16th to 30th "	11,621	6,267	125.3
" 1st to 15th December	8,100	4,246	84.9
" 16th to 31st "	5,665	3,008	60.1
" 1st to 15th January	2,857	1,424	28.5
" 16th to 31st "	1,719	893	17.8
" 1st to 15th February	909	510	10.2
" 16th to 28th "	687	332	6.6
" 1st to 15th March	266	159	3.3
" 16th to 31st "	74	55	1.1

In the government district of Oppeln the epidemics began in July, and the first marked increase appeared in August. Only Munich showed at times during November and December a greater increase

of cholera than during the previous months. Leaving this exception out of consideration, we can say that for Germany the real seasons for the spread of cholera are the summer and autumn, so that for the most part it begins or increases with the summer heat of July and August, is still on the increase until September, and decreases during the cold season. A typical example of this kind appears to me to be offered by the cholera epidemic in Hamburg in 1892. This coincided in general with the period during which a strong predisposition to intestinal catarrh existed as shown by the occurrence of cases of cholera nostras. That this period is particularly favorable to the development of cholera epidemics by reason of the ripening of fruits and the great development of putrefactive agents in other articles of food has already been frequently mentioned. For that reason it is very probable that during that time also, the cholera germs increase greatly in number and become more virulent. The fact that during the warm season slight errors of diet are frequently followed by severe digestive disturbances, is also perhaps worthy of consideration.

Nevertheless in many places winter epidemics have also been observed. The first cholera epidemic in 1830 continued throughout the winter of that year without diminution in Orenburg, despite the great cold. Furthermore, in St. Petersburg, Moscow, Bergen, Prague, New York, New Orleans, and many other places winter epidemics have been observed. In Munich the height of the epidemic of 1836 and 1837 was in November and December, that of 1873 and 1874 in December and January. In eastern Prussia cholera prevailed during the winter of 1860 in Altona and Nietleben. Epidemics occurred during the winter of 1892 and 1893.

At other times it has been observed that although cases become less numerous with the beginning of winter, in the spring and summer an increase occurred, so that with the beginning of the hot season of the year a true epidemic appears again. Koch believes that this phenomenon may be explained by the fact that the infection is transmitted from person to person during the winter, thus forming a chain of cases keeping alive the disease and uniting the apparently separated epidemics. It has not, however, yet been proven that the new epidemic has grown from such a chain of cases, and the question is still an open one whether the microorganisms of cholera, of which we shall speak further on, are not capable of wintering in temperate zones and, with the beginning of the warmer season, of regaining their virulence and the power to give rise to epidemics. But, however we may explain these occurrences, there can be no doubt that the seasonal conditions are of great importance as regards the spread of cholera.

In tropical and subtropical regions, it is not always the warmest months which show an increase in the prevalence of cholera. A considerable increase, however, tends to take place whenever large numbers of people are crowded together. Thus the religious bathing feasts, which are celebrated in India and to which many thousands travel in order to bathe in the Ganges and drink the water of the holy river, afford a most favorable occasion for an extraordinary spread of cholera. Not only are the pilgrims themselves endangered, but the disease is spread over vast regions by the dispersion of the multitude in all directions. Hankin considers the water of the Ganges less dangerous than are the tanks situated in the immediate vicinity of the river, the waters of which have been demonstrated by numerous examples to contribute greatly to the spread of cholera in India. With the opening of the Suez Canal the pilgrimages of Mohammedans to Mecca have assumed a special significance. Epidemics brought from India have frequently broken out among the pilgrims, and great numbers of cases there have been conveyed from Mecca to Egypt, and often also still further to the European Mediterranean ports. These were particularly endangered in the warm season. It is frequently assumed, and not without good reason, that the long-continued prevalence of moist heat increases the seasonal disposition. During the Hamburg epidemic of 1892, a dry heat prevailed for weeks, and in consequence the temperature of the water in the Elbe, which served for the drinking-water of Hamburg, was elevated. At the same time the low state of the river and the small amount of water which flowed from above brought it about that the sewage of Hamburg was not removed by the ordinary ebb and flow, and so the water-supply, derived from the same river, was fouled. However, the same observations were not made in all of the epidemics. Much labor has been devoted to a study of the conditions of temperature, rainfall, height of the barometer, thunder-storms, and the amount of ozone in the atmosphere as bearing upon the spread of cholera, but as yet without the attainment of any uniform results. At one time the epidemic decreased with the occurrence of rain, at another time it increased; now there was a great deal of thunder, again but little; and just as variable were the force and direction of the wind. According to this, all these circumstances can have but a subordinate and accidental significance, and for the temperate zones, the heat of the summer and autumn remains as the one definite climatic condition. It is as yet uncertain whether this warmth has an influence upon the microorganisms of cholera, or whether it influences the human body and predisposes it to suffer from the action of the germs. It is very possible that both circumstances play a part in the etiology of cholera.

Individual Conditions.

Everywhere on the surface of the earth and among all nations the experience has always been that race and nationality, as accessory factors in the spread of cholera, are without significance. It has been observed in India that occasionally the natives are attacked in greater numbers, but at another time the Europeans are the greatest sufferers, and similar observations have been made in all other parts of the world. As the various races react in the same manner against cholera, so also is no difference observed in the character of cholera wherever it appears. All over, the clinical picture of the severe as well as of the mild cases is all in all the same, although in certain epidemics some variation has been observed in the predominant symptoms. The proportion of severe cases and consequently the mortality are not the same, however, in all places. Next to the severity of the epidemic the individual disposition also plays a part in this.

And first, as to age. Nursing infants were said by the older observers to be but seldom attacked by cholera; but this relative immunity prevails only among children at the breast, and bottle-fed infants appear as a matter of fact to form a particularly large proportion of the fatal cases. At least the Hamburg epidemic of 1892 shows a high percentage of cases and deaths during the first five years of life. In the following years the predisposition sinks quite considerably, only to increase between the ages of twenty and twenty-five. Up to the twenty-fifth year, indeed, not only the morbidity is less, but the mortality is also disproportionately small. From the twenty-fifth year the morbidity increases considerably, and the mortality also increases progressively from this time.

As regards sex, the morbidity and mortality are slightly greater in women. The very astonishing observation was made in the Hamburg epidemic that the percentage of deaths among those attacked was much reduced in persons over fifteen years of age. An explanation of this might be found in the fact that the relatively favorable age of from fifteen to twenty-five years include the greater number of the unmarried. The small number of sufferers among the Jewish population in Hamburg was another very remarkable phenomenon. Inasmuch, however, as in other particularly Russian and Polish regions the cholera has often been seen to rage with special fury among the Jewish inhabitants, the Hebrew race would seem to enjoy no special immunity, and their peculiar exemption in Hamburg might be explained by the fact that among the working class of the population who were the chief sufferers there are only a few Hebrews. How

far poverty and wealth are of influence in the etiology of cholera has already been discussed above. As regards occupation also, it was shown in a previous section that the river population suffered particularly from cholera. That laundresses appear to take sick more readily was also observed in Hamburg. Laborers who were occupied only occasionally and who for the most part sought work at the harbor and found it more or less irregularly, furnished an extraordinarily large proportion of the fatal cases. As regards these persons, however, the predisposing circumstance is to be added that they mostly live from hand to mouth, at one time plentifully, at another time poorly, and on all occasions, whether of joy or sorrow, they indulge to excess in alcohol.

That Sunday is a very important day in the etiology of cholera, on account of the excesses then indulged in, was emphasized by many former authors, and was taught us anew by the Hamburg epidemic. But other occasional circumstances, accidental excesses or unusual exertion appear to call forth an outbreak of cholera among people who otherwise live hygienically. It may be assumed with safety that here the cholera germs must have already been present in the bodies of those attacked, but were temporarily not in position to set the disease free, as it were. Perhaps we can also explain in this manner the observation made in a hospital in Paris, according to which during the prevalence of cholera there, the newly operated cases were especially liable. We observed some cases in which a common source of infection for an entire family was evident, in which, however, certain members remained well until a sudden excess in eating or drinking caused the cholera to break out after a short space of time. Some who fled from a cholera city, and at their place of refuge celebrated with wine and beer their joy over the successful flight, endangered or sacrificed their lives in this manner. An excess had created the formerly non-existing individual disposition to cholera.

Next to the persons working on the river, the workmen in the gas factories showed a large number of cholera cases. A small mortality from cholera was observed in Hamburg among the workers in leather and cigarmakers, but the figures here are too small to be of any service. Cantani believes that in general tanners are immune, in contrast to special kid-glove tanners, and attributes this difference to the action of the tannic acid, which is used only in the first trade. In Hamburg the brewery workmen showed a particularly low mortality rate. As the number of these is enormous, a mere chance can be excluded. We must attribute this fact to the circumstance that the brewers drink hardly any water. Besides this, however, the Hamburg breweries use for the most part water from artesian wells.

A special predisposition to cholera and a high mortality rate are found among invalids and persons of a weak constitution. Griesinger believes that one of the grounds for the great frequency of cholera in the beginning of an epidemic depends upon the fact that a large number of cachectic, delicate, and marantic individuals are snatched away at the very first. The fact was evident in Hamburg, and it is in agreement also with the frequently observed phenomenon that after a murderous epidemic has run its course the conditions of health in a city improve and the mortality rate for a while decreases. A disease which affords immunity against cholera was not observed in Hamburg. Acute and chronic diseases were equally complicated by cholera. Even the phthisical were not spared. The cholera occurred with special frequency in individuals with a weak gastro-intestinal tract. Here also, just as in the case of errors of diet, we are probably dealing with the fact that the body does not possess the power to render inert the microbic causes of cholera. This resistant power of the body also appears to suffer by all sudden changes in the quality or quantity of food. Cold, overexertion, and other departures from normal hygiene work in the same manner. For these reasons it is that cholera also tends to decimate armies in the field. Fear of cholera can hardly be included among the individual predisposing causes. In so far as it increases the care which the person observes to avoid injurious influences, it grants rather a protection.

Of great interest is the question whether one attack of cholera affords protection against subsequent ones. This has been asserted many a time, but proof of it was not furnished by the Hamburg epidemic. On the contrary, many cases were observed in which, beyond any question, cholera had been acquired a number of times. Whether the mortality of the second attack is less, a certain protection being thereby afforded, cannot be determined from a study of the small number of observations which have been hitherto recorded.

Epidemic Behavior of Cholera.

The introduction of cholera into a city or region is followed at one time by an extensive epidemic, at another by the occurrence of only individual cases of the disease. We have already discussed above which circumstances predispose to and which tend to check the spread of the disease. If we study carefully the various epidemics, we shall be able to distinguish very clearly two entirely different forms, between which transition forms of the most varied character are found. One of these forms was designated by Koch as the chain-

like epidemic, the cases seeming to follow each other in a regular succession. This chain form suggests a direct transmission of the disease from person to person. Other observations, however, lead to the conclusion that the contagion of cholera is not one of very marked virulence. In this connection it is interesting to note the fact that a number of persons suffering from cholera with typical diarrhœa lay for many days in the midst of other patients in the hospital and did not transmit the disease to any among them. Some very typical observations of this kind were made in Hamburg. We may mention also that Grashey, as a result of a thorough study of a house epidemic in the Julius Hospital in Würzburg, also came to the conclusion that living in a room in which a cholera patient is lying does not endanger the individual in question. If, however, we study cases occurring among the attendants on the sick, which have been investigated with all the newer aids, then there can be no doubt that close association with cholera patients and resulting contamination with the dejecta can contribute to the spread of the disease. That the disease contracted in this way does not always progress to the malignant algid stage furnishes no argument against the possibility of this mode of contagion. The small number of cases arising by direct infection leads to the conclusion, however, that it is impossible for epidemics of a great extent to occur in this way.

As is well known, von Pettenkofer entirely denied the possibility of this mode of conveyance. He compared the cholera with typhoid fever in which also he rejected direct infection. Nevertheless even in regard to typhoid fever my own very extensive experience does not support the theory of von Pettenkofer. In the New General Hospital at Hamburg, from the beginning of 1887 up to December 31st, 1893, 4,106 typhoid fever patients were treated. Of this number there were 43 cases among the nurses and attendants with 5 deaths. These 43 patients were divided as follows: 2 workers in the laundry, 1 pharmacist, 3 workers in the bandage material, 1 fireman in the medical division, 1 morgue attendant, and 35 male and female nurses. It was, of course, a matter of very great interest to find out the divisions in which these nurses served. And from this examination it was seen that all of those who were sick with typhoid fever belonged to the medical division, and that in the great majority it could be shown with certainty that they were entrusted with the nursing of typhoid patients. These 35 cases, with 5 deaths, assume, however, a special significance on account of the fact that among the attendants in the surgical division not one suffered from typhoid fever. This perhaps would be attributed to a mere chance if the number in the surgical wards as compared to that of the medical side was insignifi-

cant. This, however, is by no means the case, for the proportion of surgical to medical nurses is as 101 : 116.

These facts lead to the conclusion that in typhoid fever also direct contagion may occur, but on account of the small number of such cases no extensive typhoid fever epidemics could arise in this way. Similarly, as experience shows, we must conclude in respect to cholera. By the term "direct transmission" I do not imply an immediate transference of the cholera germ to the mouth of the infected person from the dejecta of the patient through spattering or by means of some intermediate object. This can certainly occur, but it is just as conceivable that the conveyance takes place through the agency of a great number of intermediate objects. We need not insist here upon the very evident fact that in this respect cholera contrasts strongly with certain of the well-known infectious diseases and that, contrary to what is of constant observation in smallpox and scarlet fever, for example, the disease cannot be conveyed by clothing and other objects unsoiled by the dejecta. On the other hand, we must not forget that it is only in the case of very few among the contagious diseases that we know positively the mode of transmission. As regards cholera we know at least of a few ways. And first of all occurs to us the frequent transmission of cholera by means of the soiled linen. But even here the question is only as to one of the modes of contamination of food and drink by the germ of the disease. The water-supply for a long time has been regarded as a most frequent medium for cholera transmission, and besides the account of Macnamara, of which we shall speak more fully later on, there are very many observations, dating from an early period in the history of cholera, establishing the fact of the conveyance of cholera by means of drinking-water.

Even if, as von Pettenkofer maintains, some of these accounts could be explained in a different way, still a large number of observations are best explained by admitting the possibility of an infection by water. The sickness of certain communities settled around an Indian tank, the water of which, polluted by dejecta and by being used for bathing purposes, is also employed for drinking, as well as that of others lying on the banks of a river, the water of which is contaminated by the discharges of cholera patients, ought to point plainly enough to a water infection.

Infection through water which is used by a large number of people for both drinking and household purposes may be regarded as the most frequent cause of a second form of epidemic. This appears suddenly and spreads very rapidly over all the region supplied by a common source, and thus attacks a large number of persons. Hamburg might be mentioned as furnishing a typical example of

this kind. The explosive outbreak of the epidemic caused one to conclude from the very beginning that almost simultaneously a general and extraordinarily large sowing of cholera germs had taken place. As the first cases occurred among persons living and working along the Elbe and in the harbor, and then quite suddenly a severe and extensive epidemic followed, suspicion was naturally directed towards the aqueduct which brought the unfiltered Elbe water into the city. This view found corroboration in the condition of the neighboring cities of Wandsbeck and Altona, which differed but slightly, as regards situation, from Hamburg, but which had a different water-supply. While Wandsbeck draws its water from lakes, Altona water is first drawn through sand filters. And yet the unfiltered water of Altona, which is drawn from the Elbe below Hamburg, is inferior to that of Hamburg. Whereas in Hamburg 26.32 per 1,000 of the population were taken sick with cholera, and 13.44 died, Altona had—according to the account of Wallich—3.81 cases per 1,000 with 2.13 deaths; and Wandsbeck, according to Hunnius, had 3.06 cases per 1,000 with 2.09 deaths. These numbers, even if small errors in the various ways of reckoning should exist, speak convincingly, especially since the other differences are not great enough to permit of another explanation. It must be added, moreover, that of those who were taken sick and died in Altona and Wandsbeck, many had their places of business in Hamburg and its harbor, so that perhaps the infection originated there. An infection of the Hamburg water supply was, however, very probable, because it was unfiltered water of the Elbe, and contamination of the intake for the city's supply by the intestinal discharges of those ill in harbor and on board ships was very possible.

Most of the epidemics, however, did not have such an explosive beginning. These might rather be looked upon as a union of various smaller epidemics in circumscribed districts. Frequently the first cases appear scattered, and from these arise small aggregations of cases, from which a further extension takes place. In the larger cities numerous centres are formed in this manner. The more unfavorable the hygienic conditions, the more readily do they develop and the greater extension do they assume. If during the course of the slow advance climatic conditions arise which favor the development of the disease, then a very extensive epidemic suddenly appears. On the other hand, circumstances which tend to check the development may extinguish one or all of the foci of infection. If some of these areas remain, then, under unfavorable circumstances, a new extension may take place from this. Thus the various forms of the epidemic, the diversity of development, the height and decline of the same are explained.

It is of very great significance that in the countries outside of India the disease does not establish itself permanently as an endemic disease. Of course it may remain for many years in the same place, as was the case in Hamburg from 1831 to 1835, in Paris from 1832 to 1837, in Prague in the years following 1848. At times, in the course of these prolonged visitations, the disease appears to be extinct, but then suddenly a fresh collection of cases will be discovered. In general, however, the number becomes less and less, the severe cases with a well-marked symptom complex become fewer, and gradually the disease disappears altogether.

Another phenomenon which we may consider appropriately in this connection is that during the early part of the epidemic until the height of the same the mortality is usually higher than it is subsequently. The attempt has been made to explain this by saying that the weak and predisposed first succumb to the disease, but this is by no means always the case; frequently it is just the strong adults whose rapid death with very severe symptoms spreads alarm throughout the community. It might rather be assumed that in the course of time an accustoming to the infection takes place, and thereby the body acquires protection. But against this it may be replied that some people are repeatedly attacked by cholera, while new arrivals remain protected. For that reason Griesinger concludes that the extinction of the epidemic is caused by the disappearance of the specific cause.

Alongside of the severe and well-marked cases in any certain epidemic there occur many milder clinical pictures ranging from an ordinary diarrhœa to an attack of choleraic diarrhœa without the severe accompanying symptoms. These cases have been reckoned with cholera and, as we shall see later, with a perfect right. Here and there, however, an epidemic does not break out suddenly as such, but is preceded for weeks by the occurrence of many cases of simple diarrhœa or cholera nostras. These have been often looked upon as the first mild cases of the disease. In how far this is correct must be determined by later examinations. We may also mention that in an existing tendency to gastric and intestinal affections a conveyance of cholera occurs on favorable soil and may very rapidly lead to an epidemic. Still the beginning diarrhœas may be entirely absent, as was the case in Hamburg in 1892, where without preceding cases of summer diarrhœa the epidemics appeared very suddenly in an explosive manner. The behavior of cholera in the year 1893 was entirely different. Here numerous cases of diarrhœa, cholera morbus, and cholera nostras preceded the outbreak. Some of these cases, as will be explained below, could not be

regarded as belonging to cholera, others had the character of mild attack of cholera.

The duration of the individual epidemics varies extraordinarily. In the smaller places the epidemic is often entirely extinct after a few cases, or it spreads itself to the neighboring communities. Large cities are wont to be visited for a longer period. Thereby the course of the epidemic, as in all infectious diseases, is such that, after a certain period of increase the height is reached and the decline begins. It is characteristic of a cholera epidemic that even after the appearance of the disease in a severe form and a rapid rise in the number of fatal cases, the decline may occur just as rapidly. The Hamburg epidemic is a typical example of this kind. It began on August 16th with 2 cases and deaths, and by the 27th of the same month there had been 1,024 cases with 578 deaths. Then followed six days more of considerable height and then a rapid decline appeared. On the 1st of October 23 cases were reported, on the 13th 1, and on the 24th the epidemic was extinct. Similar observations have been made very frequently.

The true explanation of these epidemic peculiarities has up to the present escaped us. We are forced to think that the germs of cholera require a certain time in order to develop their great virulence, and that after reaching the height they lose in a relatively short space of time part of their infectious power.

Bacteriology.

History.

Boehm, Pacini, Klob, and Hallier made attempts to demonstrate the cause of cholera in the dejections of the patients. All these findings, however, must be regarded as inconclusive, since organisms similar to those described as the causative agents of cholera could be shown to exist in other diseases as well. Virchow in particular described in 1869 a case of arsenical poisoning, in which the microscopical examination of the intestinal contents had yielded countless masses of delicate bacteria and vibrios agreeing in every respect with the cholera fungi described by Klob and others.

During the Königsberg epidemic, Leyden believed he had found in the stools of cholera patients peculiar formations which never appeared in the fæces of patients suffering from other diseases. In the dissertation by Wiewiorowski, issued under Leyden's auspices, the organisms are described as the spores of fungi in active motion and resembling a swarm of gnats. Leyden called special attention to these findings when Koch subsequently ascribed a similar behavior to

the comma bacillus in the hanging drop. This communication induced me to investigate the subject anew. Under high powers (not oil immersion) I was able to demonstrate in some cholera cases the phenomenon described by Leyden, but I found it more frequently in cases of cholera morbus and of simple intestinal catarrh. Inasmuch as cultivation in ordinary media produced nothing but the bacterium coli, and the latter, moreover, does not give the impression of a swarm of gnats in active motion, the microorganism must be one which fails to develop on our usual media, but which cannot be regarded as the cause of true cholera. At a later period, however, cultivation in cases of diarrhœa caused the development of one of these actively motile forms, which agreed with the bacillus described by Fischer, so that at most we can say that it grows with difficulty on ordinary media.

Of course, a more accurate etiological study of most of the infectious diseases was rendered possible only by the construction of better microscopes, such as those of Zeiss and Abbé, by the use of aniline dyes, and by the introduction of improved nutrient media by R. Koch. After Robert Koch had shown by new methods and with modern auxiliaries that the cause of tuberculosis and phthisis lay in the tubercle bacillus discovered by him, it naturally followed that an epidemic disease like cholera should be studied anew with the same auxiliaries of modern methods of investigation, in order to find means to combat it. To this end, when cholera reappeared in 1883, a commission for the study of the disease, headed by Robert Koch, was appointed in August of the same year and sent to Egypt. Other members of the commission were staff surgeons Gaffky and Fischer. Owing to the subsidence of the epidemic in Egypt, the German commission proceeded to Calcutta, the indigenous centre of Asiatic cholera. The commission pursued its labors with great diligence, and their most important result was the invariable finding of a comma-shaped bacillus in the intestine and its walls, in persons recently dead of cholera. The bacillus could not be demonstrated in the blood of the heart, in the lungs, kidneys, liver, or spleen. Although these bacilli showed no definite staining reactions, their regular occurrence pointed to their connection with cholera. Even the examination in Egypt had yielded the same comma bacillus in ten autopsies on cholera subjects, while the organism was absent in other cadavers, as well as in a case which terminated fatally several weeks after recovery from cholera. Still, as Koch himself stated, there was a possibility that the bacillus belonged to the parasitic organisms regularly or frequently present in the intestines, and that the changes produced in their walls by the disease process furnished conditions specially favorable for its penetration into the tissues.

Having this point in view, the intestinal contents were carefully examined in thirty subjects dead of different diseases—ten of dysentery, two of pulmonary and intestinal tuberculosis, two of smallpox, two of remittent fever, one each of ulcerative enteritis, pulmonary gangrene with intestinal ulcers, typhoid fever, intermittent fever, leprosy, chronic bronchitis, cirrhosis of the liver, Bright's disease, contracted kidney, pneumonia, cerebrospinal meningitis, pericarditis, alcoholism, and extensive burns—but in none of the cases were the bacteria found which Koch thenceforth called comma bacilli. This investigation was not confined merely to the direct examination of the intestine, but comprised also a perfected method of cultivation by means of which the cholera bacilli had been obtained in pure culture. Contrary to this negative result, the same bacilli were found in India in the dejections of thirty-one cholera patients and were absent in only a single case in which a cholera attack had occurred seven or eight days before. Finally the bacilli were demonstrated under the microscope in the preparations from eight other autopsies on cholera subjects, some of which the head of the commission had received previously from India, and some had been forwarded to him from Alexandria by Schiess and Kartulis. The vomitus of cholera patients was also frequently examined both with the microscope and by culture; but in only two instances were cholera bacilli found in it, and in these cases the composition of the fluid indicated that it did not consist of true gastric contents but was raised from the intestine by abdominal pressure. The fluid had an alkaline reaction and presented every appearance of intestinal contents. Moreover, unquestionable comma bacilli were found in an Indian tank which furnished the water for drinking and domestic purposes to the entire neighborhood and in the immediate vicinity of which a number of cholera cases had occurred.

All these factors, together with certain peculiarities of the cholera bacteria and especially their sensitiveness to hydrochloric acid, which harmonized well with the clinical symptoms of the disease, rendered the connection of the comma bacilli with cholera very probable. On the other hand, all attempts made in India to produce the disease in animals by cultures of comma bacilli resulted in failure, but this is to be ascribed to the immunity of animals to cholera, a fact which was formerly disputed. After his return to Berlin R. Koch was able to produce infection in guinea-pigs by a different method. As experience in the laboratory had shown that hydrochloric acid inhibited the growth of the comma bacilli, Koch prepared the animals for the experiment by introducing 5 c.c. of soda solution and paralyzing intestinal peristalsis by an intraperitoneal injection of opium solu-

tion, after which cholera cultures were passed into the stomach with a probe. Thirty-five guinea-pigs were thus treated. Of these, thirty died, as Koch believes, of cholera. The symptoms were an almost paralytic weakness of the posterior extremities, feeble heart action, and tardy death. Post-mortem examination showed the small intestine to be markedly reddened and fluctuating; in analogy with the findings in man, it was filled with a watery and flocculent colorless fluid containing pure cultures of large masses of comma bacilli, as demonstrated under the microscope and by gelatin plates. The rectum still contained firm fæces, as no diarrhœa had occurred.

Parallel experiments with other bacteria, especially such as bear some resemblance to the cholera bacilli, produced some deviations from the findings noted with comma bacilli, but on the whole similar results were obtained with the Finkler-Prior bacilli and some others. If we take into consideration that the experiments were rather severe and different from natural infection, the conclusion would be permissible that while the comma bacilli undoubtedly possess energetic pathogenic qualities the etiological relations of the organisms to cholera were not placed beyond question by these experiments. On the other hand, the latter cannot be looked upon as disproving these relations, since the statements formerly made as to animals having been attacked in cholera times have not been confirmed by critical investigation, and since the proof furnished of a certain pathogenic property for animals, with the partly characteristic post-mortem finding, would of course permit the interpretation Koch put upon it. Besides, more recent investigations by Metchnikoff have thrown much light on the question of the transmission of cholera to animals. He succeeded in producing symptoms resembling cholera in man by introducing cholera vibrios with the milk into the stomach of new-born rabbits from one to four days old. Wiener repeated the same experiment with young cats, with the same result. By the simultaneous administration of cultures of the bacterium coli the effect of small quantities of cholera vibrios could be markedly increased.

However, as these animal experiments failed to produce an effect absolutely identical with cholera in man, it became a matter of great importance in establishing the etiology whether the cholera epidemics in Europe and India were confirmatory of Koch's statements, and this has indeed been the case to the fullest extent.

During the Hamburg epidemic of 1892 a thorough bacteriological examination was made by Fränkel and Simmonds in every case that came to the post-mortem table of the state hospitals. The result of the examination was that comma bacilli could be demonstrated in every fresh cadaver which came under observation within the first

seven days after the onset of true cholera. That there were isolated cases which had been diagnosed as cholera but presented at the autopsy other pathologico-anatomical processes and an absence of comma bacilli need not cause surprise. In the remaining cases the direct microscopical examination frequently showed a mixture of various species of bacteria among which the comma bacilli not even predominated in number. On the other hand, plate cultures often produced nothing but comma bacilli. They were found most abundantly in the lower portions of the ileum, though they occurred also in the duodenum and in not a few cases they were cultivated from the stomach. In some fatal cases of typical cholera we failed to find the bacilli on what we thought to be the third or fourth day of the disease; but more careful study of the history showed that the patients in question had been sick at least six or seven days, so that we regard the sixth or seventh day of the disease as the earliest period when the comma bacilli disappeared. It should be borne in mind, however, that some of these cases with negative findings had died of complications such as pneumonia, etc., and in others it is not improbable that repeated examinations including the intestinal walls might still have furnished positive results. But we were surprised to find comma bacilli still present in the intestine as late as the eighth, ninth, tenth, twelfth, sixteenth, and even the eighteenth day of the disease in forty-nine among one hundred and twenty post-mortem examinations, and these were chiefly patients who had died with symptoms of coma, with or without complications. Yet it was not only in cases with typical symptoms of cholera that comma bacilli could be demonstrated in the dejections, but also in patients suffering merely from diarrhœa without other manifestations of the disease. Similar instances have been described by Guttmann.

In the post-epidemic cholera period during December, 1892, and January, 1893, the relation of the comma bacilli could be studied more thoroughly, owing to the small number of cases, than in July and August. Altogether the bacilli were found in the dejections in sixty-two cases, among which nineteen were free from serious disturbances of the general health. The reason why these cases were examined for comma bacilli was that the persons had come in contact with cholera patients in the city and on board ship. That a few of these did not even suffer from diarrhœa has been repeatedly pointed out. Yet in one case in which no intercourse with cholera patients could be demonstrated and in which diarrhœa had existed since the 23d of February, death from cholera at the end of the month was clearly established. From that time to the 1st of June thorough bacteriological examinations were made in seventy cases of diarrhœa,

some of which came from on board ship; but the results were absolutely negative.

The investigations made by Dunbar in the newly erected hygienic institute at Hamburg likewise confirmed Koch's findings. Points of interest in his examinations are that cholera vibrios could be demonstrated in the solid fæces of eleven healthy persons who had lived with cholera patients. Furthermore, cholera bacilli could be obtained from one of the stools even after one hundred and sixty-three days, and from another after one hundred and three days. The vibrios remained alive for a considerable time at a temperature of 0° C. (32° F.). Moreover, the different epidemics during the years 1893 and 1894 removed every doubt that the comma bacilli described by Koch are the constant concomitants of Asiatic cholera.

Of great importance in connection with these positive findings in cholera are the negative results obtained in different diseases. In the New General Hospital at Hamburg three hundred and seventy patients affected partly with cholera morbus, partly with simple or repeated attacks of diarrhœa, were examined for comma bacilli during 1892 and 1893. All these examinations, some of which were continued for many days, were negative in their results. The number examined included twenty-nine cases of cholera nostras. The other diseases covered by the investigation were influenza, pneumonia, pleurisy, bronchitis, malaria, typhoid fever, Weil's disease, peritonitis, perityphlitis, parametritis, mastitis, diphtheria, syphilis, meningitis, cerebral hemorrhage, alcoholism and delirium tremens, lead poisoning, angina pectoris, tabes mesenterica, tænia, dysentery, morphinism, chlorosis, puerperal fever, hepatic cirrhosis, and vomiting of pregnancy These two facts alone should lead to the conclusion that the comma bacilli stand in an etiological relation to cholera. But this view met with a prominent opponent in the person of von Pettenkofer, whose studies upon cholera occupy a high place. At first he doubted the intimate relations of the comma bacilli to cholera, and when this position became untenable he asserted that the comma bacilli by themselves were not sufficient to produce cholera, but that this required in addition a local, temporal, and individual disposition. In order to settle this question he made an attempt at infection in his own person. On October 7th, 1892, with a view to neutralizing the hydrochloric acid of the stomach, he dissolved 1 gm. of bicarbonate of sodium in 100 c.c. of the Munich tap water, added to it about 1 c.c. of a fresh culture of comma bacilli which he had obtained from Gaffky of Hamburg, and emptied the glass at one draught; he then rinsed the glass with an additional 50 c.c. of water and drank this too. On October 9th in the afternoon diarrhœa set in, which increased during the night and caused re-

peated interruptions of sleep and broke his rest in bed. On the 10th he had five very thin stools which were partly colorless or watery.

On October 11th the stool was again colored, but the diarrhœa continued to the 15th, after which date his condition was perfectly normal. During the entire time von Pettenkofer suffered no inconvenience except some rumbling and cooing in the abdomen. Comma bacilli in large numbers were demonstrated in the thin dejections by Pfeiffer and Eisenlohr. On October 4th the fæces, which were of normal appearance, contained only isolated bacilli, and on the 16th these could no longer be found. Emmerich, von Pettenkofer's assistant, took on October 17th, 1892, in the same manner 0.1 c.c. of a flourishing comma-bacillus culture twenty-four hours old. In the evening, in order to add an error of diet to the experiment, he ate a heavy supper, during which he drank three and a half litres of strong beer. To his surprise diarrhœa with rice-water stools occurred during the same night. In the course of thirty-seven hours he had from fifteen to twenty colorless watery evacuations of from 100–200 c.c., and later twenty more stools of the same color and quantity until on October 21st, at one o'clock P.M., the first semisolid brown-colored fecal evacuation appeared. After the 22d of October the stools were again regular. Besides the diarrhœa, there were great thirst, frequent rumbling in the abdomen, somewhat hoarse voice, and a feeling of dryness in the pharynx. Comma bacilli could be demonstrated from the 18th to the 28th of October. They were present in pure culture in the colorless stools of October 19th. The urinary secretion in both experiments was apparently unchanged; it should be mentioned that von Pettenkofer repeatedly tested his urine for albumin, but with negative result.

These two cases prove unquestionably that the introduction of pure cultures of comma bacilli may lead to serious diarrhœal disease, nor need there be any hesitation to identify it with cholera diarrhœa or cholerine; but to say the least it is surprising that a quantity of 1 c.c. of pure culture did not cause the typical and grave picture of cholera, the algid stage. However, as Koch points out, such an experiment can be of decisive importance only when it is made simultaneously upon a number of persons; for the larger the number of individuals infected the smaller becomes the probability that those attacked by the disease owed their sickness to an accident apart from the experiment. I should like to add that this also excludes as far as possible the influence of individual predisposition which undoubtedly plays a prominent part in cholera.

An instance of cholera infection equivalent to an experiment is reported by Macnamara: "By an accident [the nature of the acci-

dent is not mentioned] cholera dejections got into water. This water remained exposed to the heat of the sun for a whole day, when nineteen persons drank of it, and five of these were attacked by cholera within thirty-six hours."

This report, which is rather brief, has given rise to various doubts, for which reason R. Koch took occasion to make particular inquiries about it. In a letter to R. Koch, Macnamara confirmed the fact and declared that he was ready to furnish additional details. It should be mentioned as a matter of importance that at the time and especially in the locality where this accident occurred cholera was almost altogether quiescent. Besides, all persons familiar with Indian conditions to whom the circumstances were known and who were asked concerning it had no doubt that the patients in question had been attacked as a result of the ingestion of the defiled water. This instance of the transmission of cholera is to be looked upon as one of the most significant, although it would be desirable to have all the details along with the report as to the course of the disease.

In recent times various physicians have attempted to produce infection with the comma bacilli. One of these experiments was made by Rueger of Elberfeld, without any deviation from the normal appearing in the stools or in the general health. A larger number is reported by Metchnikoff. Altogether there were twelve attempts at infection in eight persons; of these five gave positive and seven negative results. One of these experiments is cited below; it was made with old bouillon cultures from the epidemic of 1884, which had ceased to prove virulent to animals.

Nine hours after the administration of the bacilli slight colicky pains set in, followed three hours later by very watery stools. During the first and second days the stools were at first formed and then assumed the characteristic rice-water appearance. At the same time subnormal temperatures, repeated vomiting, and cramps in the calves were observed. At the end of the second day complete anuria was present. On the third day improvement began, the stools became more formed, and on the fourth day convalescence was definitive. In the evacuations of the first days almost pure cultures of comma bacilli and sparse colonies of the bacterium coli commune were noted. From the fifth day on, the latter predominated while the former decreased in number. Comma bacilli could be demonstrated as late as the seventh day, even in the solid fæces.

In this experiment the development of true cholera, though of a benign type, will hardly appear doubtful. At Stricker's instigation and under his direction Hasterlik also attempted a number of cholera

infections in man. Five of these were negative and three positive. Among the negative results bacilli could be demonstrated in the normal stools in one case. In the three positive cases the bacilli appeared on the day following their ingestion and subsequently even pure cultures were present. They could be demonstrated for several days. Severe morbid symptoms occurred in only one case and consisted of moderate fever of brief duration, very frequent and occasionally involuntary diarrhœal stools, and tenesmus. Headache, sleeplessness, weakness, and nausea were also present. In another positive case splashing sounds and visible distention of the colon were noted.

While these results differ somewhat from the ordinary picture of cholera, the pathogenic effects of the bacilli upon the intestine are sufficiently evident in the experiments. Two other attempts at experimental infection, made by Rochefontaine, of Paris, and by Wall, formerly an English military surgeon, of Budapest, proved negative.

If the objection is made to all these experimental infections that no death resulted, we may cite the fatal case of Oergel in 1874 as evidence that even in a locality absolutely free from cholera the accidental introduction of a laboratory culture of cholera vibrios may produce the typical picture of cholera and death from the disease. Therefore we are forced to the conclusion that the comma bacilli described by Robert Koch are the cause of Asiatic cholera.

Differentiation of the Cholera Vibrios.

The differentiation of the bacilli of Asiatic cholera seemed at first to present no difficulties. The peculiar form alone distinguished the vibrios from the species previously known, so that in many cases the examination of a flake of mucus from the stools, spread on a cover-glass and stained, permitted the diagnosis by the characterisic arrangement. The cholera bacilli are somewhat smaller than tubercle bacilli, but they are fuller and thicker, usually curved, and measure from 1.5–2 μ in length. In cover-glass preparations stained with an aqueous solution of fuchsin or methylene blue they often appear in corkscrew-like filaments composed of a number of individuals joined end to end. Occasionally there are associated with them large spirilla derived from the oral cavity and other bacteria from the intestinal canal. When curved vibrios occur along with other forms the diagnosis is impossible from the cover-glass preparation, for it has been ascertained that similar curved organisms are met with now and then in the absence of Asiatic cholera. Such findings have been reported by Finkler-Prior in a case of cholera nostras and by Deneke in old cheese.

Similar discoveries in doubtful cases render it necessary to isolate the curved vibrios and determine their nature. Their isolation frequently necessitates their multiplication, which is effected with special facility in alkaline fluids. When they are then examined in a hanging drop the vibrios exhibit distinct motility, due in part to a flagellum attached to one end of the bacillus, which was discovered by Löffler. A peptone cultivation also favors the multiplication and to some extent the isolation of the cholera vibrios (Koch-Dunbar). A sterilized aqueous solution of 1 per cent. of peptone and 0.5 per cent. of sodium chloride, rendered alkaline and added in amounts of one or more platinum loops to the liquid to be examined, is placed in the oven at 37° C. As Schottelius first pointed out, the cholera bacteria, owing to their urgent need of oxygen, tend to rise to the surface of the nutrient medium, where they increase luxuriantly. In from six to twelve hours after the planting of the culture we often find on the surface of the peptone solution a pure culture of comma bacilli, now and then mixed with bacterium coli. In doubtful cases a second examination is made by plate culture. The gelatin-plate culture will be first considered. The demonstration is effected by spreading a flake of mucus or a loopful from the surface of the peptone culture on ten-per-cent. alkaline nutrient gelatin and placing it in the oven at 22° C. In forty-eight hours at the latest the colonies of comma bacilli present a characteristic appearance in the shape of yellowish-white lustrous discs having a granular aspect, an irregularly indented margin, and showing marked refraction of light; the microscopical examination of these colonies must show a pure culture. Deyke recently recommended a substitute for Koch's medium, the most essential and specific constituent of which is an alkaline albuminate. This medium may be termed elective for cholera bacilli, but it permits no differentiation from certain vibrios to be mentioned hereafter. Cholera vibrios may also be cultivated upon agar plates, superficial inoculation upon which often permits their determination after from eight to ten hours at 37° C. When the colonies are transferred from the plate to a gelatin tube by a stab inoculation, the gelatin is liquefied in the shape of a funnel which sinks slowly.

The cholera vibrios grow luxuriantly in bouillon which quickly becomes turbid. Pöhl, Bujwid, and Dunham have shown that the addition of concentrated, chemically pure sulphuric acid to a twenty-four hours' bouillon culture produces a beautiful violet-red color. Brieger called the resulting pigment, which is related to indol, cholera red; but as other microorganisms furnish the same pigment, which depends upon the simultaneous formation of nitrites, the change of color was subsequently designated as the nitroso-indol reaction.

It would be desirable, however, to test the pathogenic qualities of the cholera vibrios by animal experiments, but attempts to produce true cholera in animals have not succeeded. (Quite recently, however, Metchnikoff seems to have caused death in very young sucking rabbits by introducing pure cultures of genuine cholera vibrios into the mouth. But the intraperitoneal injection in guinea-pigs of the vibrios, according to Koch and Pfeiffer's investigations, was followed by serious sickness. An injection into the abdominal cavity of a guinea-pig of 1.5 mgm. of an agar culture in 1 c.c. of sterilized bouillon causes typical symptoms of poisoning, with falling temperature and death of the animal.

The above methods seemed at first to suffice for the differentiation of the cholera vibrios. Special importance in the differential diagnosis was attached to the cholera-red reaction and to animal experiments. As late as 1893 Koch believed that among all curved bacteria that come in question in the examination for cholera none had been found thus far which could cause an equal fall of temperature and the same fatal symptoms of poisoning in guinea-pigs as those described by Pfeiffer for cholera vibrios. Further observations showed, however, that these methods did not suffice for the differentiation and that other curved vibrios gave the same results.

Thus a comma bacillus described by Rubner produced the typical cholera-red reaction; and Klein and Sobernheim could cause the same symptoms of poisoning by the intraperitoneal infection of guinea-pigs by means of various other microorganisms.

A comma bacillus which could not at first be distinguished from the cholera vibrio was found with special frequency in water-courses, etc. A discovery of this kind by Dunbar and Rumpel in the river Elbe and in the Hamburg water-supply during the summer of 1893 gave rise to numerous speculations, all the more because attacks occurred soon after in the city and were followed by an epidemic numbering altogether two hundred and two cases. As the mortality, however, was much less than that in the year 1892, it was reasonable to suspect that the comma bacilli found in the Elbe were descended from cholera vibrios undergoing slow degeneration. Koch indeed believed that further investigations would possibly permit of a differentiation of these bacilli from cholera vibrios. This view was soon confirmed in that Kutscher and at nearly the same time Oergel and Willgerodt demonstrated phosphorescence in some of Dunbar's vibrios. Rumpel subsequently thought he had succeeded in rendering cholera vibrios likewise luminous, but this statement lacks confirmation. Still the relations of these water bacteria to cholera could be entertained, since in two choleriform attacks the phosphorescent

bacilli were found in the stools. Further investigations, however, have shown that the greater portion of the comma bacilli found in water have nothing to do with Asiatic cholera, so that the above-named clinical observations would strengthen the view that these microorganisms are the occasional causes of cholera morbus.

A number of investigators attempted the differentiation of the several species. Rubner, with his pupils Cuprianow and Gosio, studied the capacity of the various vibrios of decomposing glucose and found that Koch's, Finkler-Prior's, and Metchnikoff's comma bacilli formed dextrogyre, Deneke's vibrio and one of the bacilli from water lævogyre lactic acids. Pfeiffer pursued a different course. Lazarus having discovered that the blood serum of persons convalescent from cholera inhibited the development of the rapidly fatal intraperitoneal cholera infection of guinea-pigs, Pfeiffer showed that during the immunization of animals against subcutaneous and intraperitoneal cholera infection anticholeraic bactericidal substances were formed in the blood and were present in the serum. On injecting a corresponding dose of a cholera culture with the serum of an immunized animal into the abdominal cavity of a guinea-pig, the cholera bacteria perish in the peritoneal cavity in about twenty minutes and the fatal symptoms are prevented, while a like dose with ordinary serum kills the control animal. When the culture injected with the immunized serum was not one of true cholera no protecting influence was exerted.

These statements were doubted by many observers, but were confirmed by Dunbar. The latter and Pfeiffer subsequently proved that similar specific relations between the antibacterial protective substances developing during immunization and the bacteria employed for the purpose are not confined to cholera, but that analogous conditions prevail with other species of vibrio, as those of typhoid fever and the bacterium coli, and that this in fact constitutes a law of immunity. The question was afterwards reëxamined by Löffler, Flügge, and Fränkel, who agree that Pfeiffer's method furnishes a reliable diagnostic point for the differentiation of cholera bacilli.

Gruber recently offered a different explanation for Pfeiffer's discovery. He observed in the test tube that the cholera bacilli in the serum of animals immunized against the disease underwent clumping, adhered together, and assumed a different superficial aspect. He therefore believed that the specific serum acted by dissolving the capsules of the bacilli. Owing to this solution the animal organism was enabled to destroy the bacilli by its own protective powers. Pfeiffer does not accept this view, but looks upon the phenomenon as an arrest of development and upon the active substances as paralysins.

Whatever form the theoretical interpretation may assume in the future, the fact remains, as Pfeiffer points out, that when the bacilli in question are examined in cholera serum a very probable conclusion may be drawn from the occurrence or non-occurrence of clumping and agglutination as to whether the serum has an influence upon the bacilli and whether these are cholera vibrios. The action of the specific serum upon the vibrios may also be observed under the microscope. Still it would be desirable to see further proof by means of Pfeiffer's reaction in the peritoneal cavity of the guinea-pig; for the process to be observed in the test tube or under the microscope on adding the serum of animals immunized to cholera to the vibrios is not entirely identical with that occurring after the injection of cholera vibrios together with serum into the abdominal cavity of guinea-pigs. In the animal body much smaller doses produce an effect which ends in the destruction of the vibrios. Besides, in these attempts at differentiation we must bear in mind that the virulence of the cholera vibrios is not constant and that this fact may be the source of errors. It may be of interest, too, that Achard and Bensaude during the last Egyptian epidemic examined fourteen cases of cholera and observed the agglutination of the vibrios in the serum of thirteen.

The Cholera Vibrios in their Relation to the Local, Seasonal, and Individual Predisposition.

We have seen in the beginning of the section on etiology that cholera follows human intercourse and that even healthy persons may transport the germ of the disease. Bacteriological investigation has taught us that the cholera vibrios may be present about three weeks in the intestine and the dejections of apparently healthy individuals and may during this time produce the symptoms of cholera in the host when digestive disturbances supervene. Kolle even found on the thirty-third and forty-eighth day after the onset of the disease cholera vibrios in the fæces of persons who had recovered from it. The same person may, however, without being himself attacked, transport cholera vibrios which gain access to the gastrointestinal canal of other individuals. In like manner linen soiled and moistened with the dejections may effect the transmission. In this respect great interest attaches to the findings of Dunbar, who was able to cultivate viable cholera vibrios from the stools after more than three months. In this way anything that may have come in contact with the dejections is likely to become a source of infection; but this danger is lessened by the fact that drying kills the vibrios. Therefore perfectly dry linen, dry rags, letters, and dry articles of any

kind cannot serve to spread the disease. For the same reason currents of air in which only dry particles float have no influence upon the transmission. When the articles are moist the vibrios may remain viable unless they are overwhelmed by other microorganisms present at the same time. Transportation into the intestinal canal with consequent cholera, however, seems but rarely to result from the direct transfer of dejections into the mouth. The study of several house epidemics, each comprising a number of successive cases, suggests rather that certain intermediate bodies permit an increase of the vibrios transferred from the dejections. In this connection it is a matter of interest that cholera vibrios were found viable for eight days in boiled milk and upon meat, for four to six days upon butter, and for twelve days upon cauliflower and fruit. We do not know all the media by which transmission is effected, but these examples suffice to indicate several ways. Often the fingers, especially those of children, may effect the transfer. Flies and insects in general should also be thought of. A striking example of one mode of transmission was observed in a small dwelling in Hamburg, where recently washed cholera linen was hung to dry over the hearth and the pots. Close quarters and crowding, therefore, must in this respect furnish the best field for the spread of the disease germs. Moreover, as the cholera vibrios remain viable much longer on moist objects, it is not surprising that the epidemic is usually more severe in damp and low-lying parts of the city, owing to the less thorough drying of all kinds of utensils. The chain forms of epidemics in particular are apt to arise in this way, and their spread is naturally influenced also by the individual predisposition of the inhabitants. Given a number of such chains, the formation of secondary foci, and a prolonged duration of both, and the epidemic may become quite extensive.

Larger epidemics with rapid rise of the number of victims, however, are particularly likely to develop when the cholera vibrios gain access to alimentary substances which are used at the same time by many persons. Foremost among these is the drinking-water and to a less extent the water of rivers, lakes, etc. In 1884 Koch first succeeded in demonstrating the cholera bacillus twice in water from a tank in Calcutta. Since then numerous similar findings have been reported. Although some of the forms discovered were not true cholera vibrios, still many of the vibrios found were shown to be identical with Koch's cholera bacillus. Dunbar in particular has done praiseworthy work in the elucidation of this question.

The result with reference to an epidemic will be proportionate to the measure of use of the infected water by the people living near and travelling upon it. When some wells are infected, more or less exten-

sive groups of the disease develop around them. On rivers and canals the raftsmen and boatmen, who often draw water for their use from them, are specially endangered. The cholera vibrios are carried along by the current, by the vessels, by the bilge water (Lubarsch), and by the inmates of the boats. The epidemic is liable to assume large proportions especially when the river water is used for drinking and domestic purposes by a more or less numerous population. This will explain epidemics such as those of Hamburg, of the Insane Asylum at Nietleben, of Stettin, and of Niedczwedczen. Many of these, as it were, explosive epidemics present a characteristic feature to which attention has been called above. They often begin with attacks of vomiting and diarrhœa which at first do not present the picture of Asiatic cholera. Within a short period the form of the disease becomes more serious, the mortality rises, and after some time the grave attacks diminish in like manner. The same peculiarity shows itself frequently also in the chain form of the epidemic. The attacks of vomiting and diarrhœa that often mark the onset of an epidemic might be ascribed to the fact that they were produced by other causes than the vibrios of Asiatic cholera and that the epidemic when then introduced had fallen on a specially favorable soil. This, however, would not explain the same phenomenon at the decline of epidemics. Moreover, the bacteriological examinations of recent years have shown that even the initial attacks of vomiting and diarrhœa were caused by cholera vibrios. Therefore the gradual increase and decline of the mortality must be explained in another way. It appears most natural to suppose that we have to deal with changing conditions of the vibrios. There can be no doubt that the several cultures present material differences in this respect. The autoinfections and animal experiments decidedly favor this view. It may also be called to mind that Bonhoff in a series of experiments found that the intraperitoneal infection, continued from animal to animal, presented features corresponding to the course of an epidemic, since the same dose was followed by an increase in the severity of the symptoms and then by a gradual decline. The conclusion seems justified that similar results may follow the passage of the vibrios through the human body. Now and then the bacilli appear to acquire a high degree of virulence in the water. This will be the case especially when the organisms meet with conditions similar to those peculiar to their home. Several years ago I called attention to the temperature of the water, which when it is high coincides as a rule with the outbreak of cholera in Europe and particularly in Germany. It is true, Dunbar observed that when the cholera vibrios remain long in water they change decidedly in their

morphological and cultural relations, while Dunham was able to demonstrate the vibrios only for six days in infected Spree water. However, it is certain that in our experiments we cannot reproduce all the conditions which are active in nature. Moreover, the cholera vibrios are with comparative facility crowded out by other microorganisms, and this fact might also be pleaded against the relations of cholera to the water in India. Still, according to all epidemiological experience we are forced to suspect that there are other conditions besides warmth that favor the development of the vibrios in water. Thus, we might suppose that at times a number of living organisms may perish in the water and that their death possibly may furnish room and nutrient material to the cholera vibrios. Whether the latter pass through special stages of development outside the animal body in the water will have to be determined by future investigations.

The introduction of the cholera vibrios into the gastrointestinal canal is not always followed by the onset of the disease. There are many experiences in favor of the fact that a large percentage of persons are infected without presenting any results. The protective powers of the body will give battle to the foreign germs and their toxins. When the former are weaker or become so in the course of the struggle disease must follow. The protective powers of the body, however, are greatly reduced by every disturbance of the gastrointestinal function. In this respect the fall season which supplies fresh fruit is an element of special danger. On the one hand the cholera germs are easily introduced with the raw fruit, and on the other hand the plentiful ingestion of fruit is apt to lead to digestive disturbances. Besides, the number of germs in the water usually increases in autumn, thus again damaging the digestive canal. If these factors are active when the cholera germs are introduced the soil is most favorable for the development of the disease. In like manner as the ingestion of unsuitable and excessive food, colds may act injuriously on the digestive function, thus creating a predisposition. It needs no argument to prove that the individual tendency and the protective powers of the body likewise play their part. Poverty and wretchedness and some antecedent illness as a rule impair the protective powers, and the abuse of alcohol acts in the same way.

It is doubtful whether the cholera vibrios are aided in producing the disease by the simultaneous presence or introduction of other microorganisms in the gastrointestinal tract. Buchner has formulated a diblastic theory based upon this idea. Nencki has expressed himself to the same effect on the strength of some isolated findings in Russia. It may be asked whether this theory is still required to

explain cholera epidemics after what has been discovered. The reply depends upon the answer to the question whether any special and notable discoveries have been made in cholera which could be utilized in support of the diblastic theory. This question must be answered in the negative.

Thus far no protozoa have been demonstrated in the recent dejections of cholera patients. Altogether no discovery has been reported which could be interpreted in the sense of a constant occurrence of other microorganisms along with the comma bacilli. The only microbe that occurred frequently is the bacterium coli, which is usually harmless, though it may occasionally become virulent. Are we to assume that this microorganism suddenly becomes virulent under the influence of the comma bacilli and has a share in the development of cholera? Pfeiffer's investigations at least suggest the idea and Wiener's results might be interpreted in the same way. Further experimentation may clear up this question.

One important point remains to be discussed, namely, the frequent occurrence of cholera nostras by the side of Asiatic cholera. In the fall of 1892 Fürbringer described a case of this kind, which at first appeared like Asiatic cholera but after thorough bacteriological examination had to be classed as cholera nostras; a similar observation was reported by du Mesnil. Both cases ended fatally. Whether the cases observed in 1893 by Carp in Wesel, which were described as cholera nostras on the strength of bacteriological examinations made by several physicians, were really instances of that disease is doubtful, since five of the six cases were fatal.

The frequent occurrence of cholera nostras by the side of Asiatic cholera cannot, however, be denied in view of the experiences at Hamburg. Even in the secondary epidemic during December, 1892, and January, 1893, some striking examples were observed. They were briefly discussed by Rumpel. In the spring, summer, and fall of 1893 twenty-nine similar cases were observed in the New General Hospital, two of which were fatal. The most thorough bacteriological examination failed to disclose comma bacilli in these cases. Such a large number of cases of cholera morbus with two deaths is truly remarkable. At all events a search of the records of former years and inquiry among older physicians of the hospital showed that such cases were in the past very rare in Hamburg. I myself in a practice of a good many years' standing, like Fürbringer, have seen only isolated cases of grave cholera morbus with symptoms resembling those of Asiatic cholera. It might be supposed that in some cases of this disease occurring coincidently with Asiatic cholera the attack and fatal result may have been caused by very virulent comma

bacilli which had perished, so that the intoxication was the essential feature. This supposition would also agree with the post-mortem findings in such cases as differ in no way from those of Asiatic cholera. But it must be remembered that cholera morbus may present the same pathologico-anatomical conditions, although occasionally some deviations are met with in the intestines. Besides, the fact that similar cases with the same grave symptoms occur in the absence of true cholera makes it unnecessary, to say the least, to refer the disease to dead comma bacilli. The most important factor, however, seems to me this, that the cases of cholera morbus which have been observed begin with equally profuse diarrhœas, and that the recent evacuations contain here and there an extremely large number of different microorganisms, the algid stage developing only after the profuse diarrhœas; while in a primary intoxication the onset of this manifestation is to be expected earlier. For this reason we must also consider whether other, usually almost harmless parasites, which are present in the intestine or have invaded it, may not assume an extraordinary virulence under unknown conditions or under the influence of cholera vibrios.

A violent attack of cholera is often followed by a comatose stage, formerly known as cholera typhoid. As this occurs also in cholera nostras, though more rarely, it cannot be ascribed to the effect of cholera vibrios. However, as numerous cholera bacteria were usually found in the dejections during this late stage it was reasonable to assume that their toxins, together with the absorption of the decomposition products by the mucous membrane deprived of its epithelium, aided in the development of the condition.

The decline of the epidemic has been ascribed by Koch and his pupils in part to the fact that recovery from even slight attacks confers some degree of protection. But it was frequently observed in Hamburg in 1892 and 1893 that some persons had several attacks of cholera. Other factors, therefore, must be active. Increasing care and cleanliness of the population and the advancing season may play a part; the main cause, however, must lie in the fact that the vibrios disappear or gradually become less virulent. Still it is not improbable that they live through the winter months in an attenuated state and on finding favorable conditions again produce grave disease.

Hamburg was free from cholera for three and a half months in the year 1893. Then without a new importation and despite the observance of the most careful hygienic measures and the endeavor of medical men to destroy all possible connecting links with the past epidemic, the disease broke out afresh. Occurrences of this kind in cholera epidemics have not hitherto been satisfactorily explained by

bacteriological investigations. In Hamburg every case of diarrhœa in the city or the harbor was watched most carefully and was examined as to the presence or absence of cholera bacilli in the stools. Many thousand examinations of the discharges had given a negative result. Then, after three and a half months of freedom from cholera, at the end of June two cases of the disease occurred in the harbor; these could not be referred to a new importation. Now there was another pause of two months' duration, at the expiration of which, in the latter part of August, another epidemic of slight extent broke out. At this time the temperature of the Elbe water had risen to 20° R. (77° F.), and in consequence of a break in the pure-water aqueduct, unfiltered Elbe water was supplied to the city. This small epidemic, of one hundred and fifty-one cases with a mortality of 27.8 per cent., could not, as far as the most careful investigations went, be attributed to a fresh importation of cholera bacilli. Its origin was to be searched for in Hamburg itself, and its connection with the epidemic of 1892 could not be denied. All investigations again pointed to the Elbe as the source of infection. In this water the cholera germ must have passed through a stage of development which most probably consisted in a multiplication of the bacilli in consequence of the increased temperature of the water or of some other favorable change. It is not beyond the range of possibility, however, that further investigations will reveal to us the existence of a true developmental stage in the life history of the cholera bacillus, such as von Pettenkofer insists is necessary to the satisfactory explanation of the outbreak of an epidemic of Asiatic cholera.

Incubation.

It has been stated above that some persons were attacked by cholera a few hours after an excess in eating and drinking. In most cases this occurrence might be explained by the fact that the germs were already present in the body but that favorable conditions were lacking to enable them to produce the disease. As a rule more than twenty-four hours elapse between the introduction of the bacilli and the outbreak of the attack. According to the epidemiological observations by von Pettenkofer the incubation lasts from two and a half to five days, in other cases from seven to eight days. However, all these statements are uncertain. While it could be ascertained when a traveller arrived in some location and when the first attacks occurred, it was altogether impossible to determine on which day the disease was transmitted.

This and many other points in reference to the etiology and

course of cholera could be explained only after the cholera vibrios had been discovered. Then the late outbreak of the disease after excesses in a fugitive was made clear by the long sojourn of the vibrios in the system. Moreover, we learn from Emmerich's auto-experiment, who combined the introduction of comma bacilli with an error in diet, that the first loose stools occurred after from thirty-six to forty hours, while in the case of von Pettenkofer about fifty-six to sixty hours elapsed until the first symptoms appeared. Therefore it is not possible to determine a regular period of incubation from the moment of infection to the occurrence of symptoms as in other infectious diseases. The shortest period of incubation may probably be stated as thirty-six hours; but as a rule a longer time will elapse before the consequences of the introduction of cholera bacteria into the body will manifest themselves.

Pathological Anatomy.

Cholera is essentially a poisoning of the system with the toxins of the comma bacilli. Accordingly the disease has this in common with other intoxications, that the pathologico-anatomical findings present a certain disproportion to the gravity of the morbid picture. Only the point of entrance of the toxin presents a few special peculiarities in comparison with other diseases. With rare exceptions, the external appearance of a cadaver from the algid stage is indeed rather unusual. The body decomposes slowly; the integument has generally a dusky grayish-blue color; the lips, eyelids, fingers, and feet are frequently bluish-black; in the sunken pale face the half-open eyes surrounded with blue rings appear striking; the eyeballs look withered; the skin is lax, furrowed, and is easily lifted; the abdomen is usually retracted and of doughy consistence.

Other notable features are the marked rigor mortis, the fencing attitude of the limbs, the often pronounced curvature of the fingers, all of which are most distinct in younger subjects and when death has been rapid. Post-mortem twitchings are also very frequent under the same conditions, and terrify the relatives and domestics. Those who have succumbed in the later stages of the disease present no external peculiarities and particularly the manifold exanthemata which are so often observed during life are generally no longer visible at the post-mortem table.

The *subcutaneous cellular tissue* is dry; quite exceptionally only were phlegmons (inflammatory processes following infusions) found during the extensive Hamburg epidemic; these of course had nothing to do with cholera.

The *muscles* exhibit no marked change on ordinary inspection. E. Fränkel was unable to demonstrate any alteration in the muscles of the abdomen and thigh even under the microscope. On the other hand, Boltz found degenerative changes in the muscles of the larynx and diaphragm. In the most pronounced cases very many of the muscular fibrillæ had lost their transverse striation and in their protoplasm a marked, albuminous, finely granular cloudiness could be recognized. Alongside of these most numerous greatly degenerated fibres were others with distinct striation and transitional forms. In some preparations Boltz could discover nothing pathological in the muscle bundles. These changes were noted by Boltz in the muscles of the larynx, especially the internal thyroarytenoid, the diaphragm, and also in the gastrocnemius. These muscular groups did not always participate equally in the disease; sometimes the diaphragm, sometimes the laryngeal muscles were most affected. In general, the degeneration seemed to be more frequent and pronounced in cases of moderately rapid course than in those which were speedily fatal. In one autopsy made on the fifteenth day after the beginning of the disease, marked degenerative changes could be demonstrated in the muscles examined. Boltz thinks it probable that, in analogy with other infectious diseases, the result was to be ascribed to a direct action of the cholera poison upon the protoplasm of the muscular fibre.

The *central nervous system* as a rule presents no material alteration; it is often stated to be very rich in blood. The respiratory organs frequently showed lesions in the Hamburg epidemic. Among 400 lungs examined there were 13 typical lobar and 65 lobular pneumonias, that is, nearly twenty per cent. of the cases contained inflammatory processes in the lungs. This complication could be demonstrated on and after the third day of the disease. The bacteriological examination in cases of fibrinous pneumonia proved the presence of pneumococci; the lobular areas contained patches of purulent disintegration which were now and then multiple and racemose in form. In many of our cases pulmonary œdema was also observed, as were hemorrhages in the lung tissue; the latter were more frequent in the patients treated with infusions than in the rest. The air passages are to a great extent reddened and filled with mucus; proliferations of the thrush fungus on the laryngeal and pharyngeal mucosa and mycotic ulcerations may be met at the same time. In one of the cases at Hamburg laryngeal and pharyngeal diphtheria with Löffler's bacilli was demonstrated.

The *pleura*, too, is often the seat of smaller and larger hemorrhages, and of course may show every condition found in patients suffering from chronic diseases who have died suddenly.

The *pericardium* contains, in the great majority of cases from the first stage of the disease, numerous hemorrhages on the surface, particularly at the base; these are more rarely isolated and circumscribed, when they may reach the size of a lentil. It is unusual for the hemorrhages to be larger, and quite exceptional to see them extend as far as the external pericardial layer. In the second and third weeks of the disease recent hemorrhages are not often demonstrable. The heart muscle rarely contains hemorrhages, but frequently presents considerable degeneration of the muscle fibres with slight granular cloudiness. On the whole the right heart contains much more blood than the left, but it does not differ from the normal.

The chief interest attaches of course to the changes in the peritoneal cavity and the *gastrointestinal canal.* In those who have died during the actual attack the peritoneum of the small intestine is rosy red in color, with marked vascular injection, and in most cases presents a slippery surface caused by a viscid exudate. While this condition of the peritoneum possesses no pathognomonic importance (according to E. Fränkel the same phenomenon is often observed in children, especially those who have died of marasmus), it is apt to lead one to suspect cholera. However, the absence of this condition allows no conclusion to be drawn, for among 530 autopsies performed in Hamburg, in which special attention was directed to this point, it was lacking in 39. The fulness of the intestinal loops is variable; empty convolutions alternate with others filled to the point of fluctuation and whose turbid white contents glimmer through the walls. Not uncommonly we find, in subjects who succumbed during the actual attack, agonal invaginations of the small intestine, which are sometimes single, sometimes multiple. The intestinal contents of the same class of subjects have long been designated, and appositely, as rice-water-like. Still, deviations from this appearance are met with; the contents may be stained especially by bile and blood. In other cases the intestinal contents present nothing characteristic, but are simply those of ordinary diarrhœa and do not offer the slightest basis for the diagnosis "Asiatic cholera." After the fifth day of the disease the so-called typical rice-water-like intestinal contents were no longer found. The reaction of the contents, in the portions of the small intestine nearest the stomach and as far as the beginning of the jejunum, was often decidedly acid, but farther down increasing alkalinity appeared, and the liquid contents of the colon had an alkaline reaction without exception. The intestinal mucosa varies in color from the normal to a diffuse reddening with succulence or to a blackish-red bloody suffusion. Leaving the latter out of consideration, we may recognize even in the apparently slightly changed bowel that

the mucous membrane is deprived of its epithelium over large sections, that the solitary and sometimes the agminated follicles are swollen and blood-stained with small hemorrhages mostly situated in the centre of the follicles. The blackish-red bloody suffusion is met with as a rule in a later stage of the disease, in connection with diphtheritic alterations of the intestinal mucosa which may sometimes be confined to the small intestine, especially the lower ileum, sometimes to the colon or to the latter and the adjoining ileum. These necrosing affections of the mucosa are often associated with hemorrhagic processes and give rise to eschar formation and wide superficial ulcerations of the submucosa. In these cases the intestinal contents, which are otherwise of a yellow or spinach color after the cholera attack has run its course, are dirty brownish-red and offensive. It might be supposed that these diphtheritic processes in the bowel are due to the liberal use of calomel in cholera, but in that case the process should be restricted mainly to the colon, while in most of our autopsies isolated or confluent areas were found only in the small intestine.

Inflammatory changes in the peritoneum are to be found in the regions where the necrotic process of the intestinal mucosa extends deeply, and rarely in its absence.

An interesting and much disputed question is, whether the exfoliation of the superficial epithelium is a product of cadaveric maceration or whether it is a vital process due to the specific causes of the disease or their toxins. E. Fränkel has occupied himself specially with this question, and he succeeded in demonstrating, on a portion of the bowel which had been fixed in absolute alcohol within one and a half hours after the death of the subject, that by far the largest part of the superficial intestinal epithelium was exfoliated even in the most recent cases of less than one day's standing; only between some isolated villi small remnants of epithelium were preserved now and then. I have inspected these specimens and fully agree with E. Fränkel that this exfoliation of the intestinal epithelium is a vital process which must be regarded as an effect of the specific activity of the comma bacillus. The tissue changes in the bowel of cholera subjects present the typical picture of a coagulation necrosis of the villi, affecting sometimes only their tips, sometimes their entire extent, without any inflammatory infiltration with small cells. The definite temporal connection of these phenomena with the beginning or the duration of the disease could not be established. The same changes could be demonstrated both after twenty-four hours and after nineteen days' duration of the disease.

The cholera bacilli, as R. Koch first reported, are found not only

on the surface but also in the interior of the bowel, partly in the more or less necrotic villous tissue, partly in the submucosa and in the lumina of the glands of Lieberkühn. The bacilli as a rule are gathered in swarms, although the inexperienced will not always find them readily.

The diphtheritic process in the intestine shows histologically a profound mortification of the mucous membrane, with serous infiltration and swelling of the submucosa and muscularis, dilated and tensely filled vessels, areas of small-cell infiltration in the submucosa, and large numbers of many different microorganisms in the necrotic and œdematous tissue. Among these bacteria comma bacilli could also be demonstrated by culture. Commencing diphtheria of the small intestine showed extensive hemorrhagic infarction of the villi, while the multiple diphtheritic ulcers of the colon were sharply demarcated from the healthy tissue by a distinct wall of small-cell infiltration.

The condition of the stomach rarely presents any characteristic features. The reaction was sometimes alkaline, sometimes acid, even after rapid death in the algid stage. The contents were often abundant. Now and then the stomach showed changes similar to those in the intestine, with immigration of comma bacilli into the hemorrhagic or necrotic mucous membrane, so that the above-described alterations in the intestine may begin in the stomach.

The *spleen*, in the majority of cases, seems to participate but slightly in the morbid process. Some swelling indeed was found in isolated cases, without any complicating cause. Multiple hemorrhages, from a lentil to a hazelnut in size, were more often observed. Histologically the spleen presented nothing abnormal; comma bacilli could not be demonstrated either in sections or by culture. When the cholera was complicated with typhoid fever or pyæmia, the typhoid bacilli or streptococci could be demonstrated without difficulty.

Examination of the *liver* shows no essential changes, aside from accidental complications. Here and there slight cloudiness of the parenchyma was noted. The gall-bladder contains during the first days of the disease a small amount of viscid dark bile; the latter becomes thinner and often lighter in color during the following days, and in the second and third weeks of the disease the secretion is frequently light yellow. Exceptionally we may find cholecystitis with swelling, injection, and small ecchymoses of the mucous membrane and turbid purulent contents of the gall-bladder, such appearances not finding their explanation in some complication.

The involvement of the *kidneys* in the cholera process was studied

in the Hamburg epidemic by E. Fränkel and myself. Quite early, four, five, eight, and nine hours after the onset of the disease, the kidneys are seriously implicated. At this time the organs show no deviation from the normal on macroscopic inspection; they are not enlarged, grayish-red, not anæmic, and the cortex is not widened. At most the convoluted tubules may appear rather cloudy. The microscope reveals important changes consisting in foci of very marked swelling of the epithelia of the convoluted tubules. These largely exceed the normal in size, and the cell bodies directed towards the lumen are chiefly involved in the swelling. Soon additional changes may be noted in that this part of the protoplasm becomes remarkably loose and perforated like a sieve. At the same time the outlines of neighboring cells are obliterated, and those situated opposite each other approach until they touch; at such points the walls of the tubule appear crowded apart and its diameter is considerably increased. As is shown by the use of nuclear stains, the nuclei of some of these cells are dead. These are all the changes found in the kidneys at the earliest period of the disease and they recurred in typical form in three cases examined by us; only differences in degree could be noted with reference to the intensity of the swelling and shattering of the protoplasm.

An altogether different picture was presented by the kidney of a man, aged forty-five, whose disease, as we learned subsequently, was extremely violent and lasted about ten hours. The microscopical examination demonstrated a necrosis of the nuclei of the greater portion of the epithelia in the convoluted tubules, though the cells were not materially changed in form or size. The appearances agreed exactly with the description given by Klebs in his "Allgemeine Pathologie" of the kidney in cholera.

But it should be clearly understood that this condition of the renal parenchyma is of exceptional occurrence both in subjects succumbing during the actual attack and those dying at a later period, and that the characteristic changes are those involving the protoplasm of the cells. This protoplasm proves to be most intensely affected also at the end of the first and second days of the disease; but as the morbid process sets in in the earliest stages, the changes then have spread more diffusely. We had an opportunity of examining the kidneys of a man, aged forty-six, who had died exactly twenty-four hours after the outbreak of the attack and at that time hardly any unchanged cortical epithelia could be found.

The portions of the protoplasm directed towards the lumina of the tubules undergo further alterations about this time. The original loosening does not persist, but the swollen protoplasm begins to

disintegrate—a process termed by Klebs plasmolysis, as opposed to karyolysis. Even such kidneys, of which we had at our disposal for microscopical examination those from six cases, need not present any material changes on naked-eye inspection. On the other hand, the kidneys from the second to the fourth day of the disease are usually decidedly enlarged and notably full of blood, so that the cut surface has a saturated dirty grayish-red color which often changes to a dark red tint about the limiting layer. The latter is characterized under the microscope by a tense filling of the glomerular and intertubular capillaries; besides we sometimes observed larger arterial and venous branches equally full of blood. About the same time the plasmolysis has advanced farther in the secreting parenchyma, in that the portion directed towards the lumen, which was at first swollen and loosened until it resembled a sieve or net, is detached from the part containing the nucleus and adjoining the tunica propria, filling the interior of the respective urinary tubule more or less in the shape of an extremely finely granular mass for a greater or less distance. Associated with this is the occurrence in varying numbers of chiefly hyaline or coarsely granular casts which block the convoluted tubules, Henle's loops, and some of the straight canaliculi. The casts are not rarely surrounded by a ring of the finely granular material resulting from the dissolution of the cell protoplasm.

Along with these processes confined to the cell protoplasm we observe less pronounced necroses of the nuclei; these were conspicuous and spread over larger portions of the cortical epithelium in only one of the cases examined by us. In the same case, that of a woman, aged forty-five, who had died two days after the onset of the disease, the plasma degeneration was far advanced. In all the other kidneys from the same stage of the disease the latter degeneration preponderated and was found equally marked in the kidneys from the later stages of the morbid process.

The kidney affection has approximately reached its height about this time. No other changes involving additional tissue elements of the kidney occur in this, the so-called stage of reaction. It would simply be a repetition were we to describe fully the changes discovered in the various kidneys from this period; suffice it to say that, as in kidneys from the third and fourth day of the disease, those from the seventh to the twelfth day (nine kidneys from this period were examined) show the same finely granular mass, resulting from the disintegration of the protoplasm detached from the nuclear portion, in the lumina, partly mixed with refractive granules. The same remark applies to kidneys from the thirteenth, fourteenth, and fifteenth day of the disease respectively. A slightly different result was obtained

in only one case, that of a man, aged thirty-four, who had died on the eleventh day, in which the epithelia were enormously swollen and a marked fatty change had occurred in some of the cells, whose nuclei were well preserved. Even here the finely granular masses of detritus in the interior of the convoluted tubules were not lacking. While, as the above description shows, the microscopical appearance of the kidney of cholera is rather monotonous, different changes evident to naked-eye inspection develop: the saturated red tint of the outer and cut surface prevailing between the second and fourth day becomes more grayish-red or yellowish-red and gradually changes to an almost pure yellow color of the surface in many cases. In sections this last color is confined wholly to the cortical portions, while the medullary cones retain their dark red tint, which then sharply contrasts with that of the cortex, even in the later stages. The size of the organ at the same time is variable; in most cases it exceeds the normal, mainly owing to the widening of the cortex. Thus a careful macroscopical inspection permits an approximately correct estimation of the duration of the disease, and during the epidemic we were able, in some instances in which the history was incomplete, to form fairly accurate opinions.

After the third week of the disease the processes affecting the secretory renal epithelium seem to undergo involution, and accordingly the kidneys from this period present nothing worthy of note on naked-eye inspection, aside from some cloudiness of the cortex which is hardly wider than normal. We had at our disposal two kidneys from this period, from the eighteenth and nineteenth day of the disease respectively, and one from a still later period, *i.e.*, the twenty-eighth day. Under the microscope such kidneys show some remnants of the granular detritus, very rarely perhaps a few hyaline casts or a more friable material in the lumina of the convoluted tubules, here and there also a cell with necrotic nucleus, while the epithelial cells in the main are again well formed and provided with a normally high protoplasm. The regeneration, therefore, proceeds rather rapidly—a fact which may perhaps be explained by the preservation of that part of the cell body that contains the nucleus; this undoubtedly also inaugurates the restitution of the disintegrated protoplasm. We have never observed processes indicating an involvement of the vascular apparatus of the kidney and its interstitial tissue, or productive processes in the epithelium of any of the tubules. It is the absence of such changes that explains the relatively rapid restitutio ad integrum and the non-occurrence of consecutive conditions in the renal parenchyma.

Besides the above-described changes in the kidneys, other altera-

tions are met with as accidental or associated conditions; such as embolic infarctions following thrombosis in the veins into which salt infusions have been made, and more rarely small metastatic abscesses.

The *bladder*, owing to the anuria existing in the first few days, is at that time nearly always much contracted and either empty or encloses some drops of urine which is generally turbid and contains hyaline and finely granular casts. Isolated cases occur, however, in which the bladder is moderately or quite filled. On and after the third day more or less abundant and usually clear urine is found; bloody urine is an exception. The mucosa of the bladder frequently presents small hemorrhages, but extensive necrotic processes are very rare.

The *uterus* in adult women after puberty as a rule shows a peculiar pathological process. There are more or less profuse hemorrhages into the free lumen of the uterine cavity. At the same time the superficial layers contain hemorrhagic infarctions; but the simultaneous effusion of blood into the Graafian follicles which characterizes menstruation is usually absent. The microscope discloses hemorrhagic infarction of the uterine mucosa, usually penetrating deeply, together with great dilatation and injection of the vessels and often also abundant fatty granular cells (mast cells), like those occurring in the mucous membrane of the stomach and bowel. This alteration of the uterine mucosa might explain the fact that cholera in pregnant women very often causes abortion or premature labor. The hemorrhagic infarction seems to cause the detachment of the membranes and thus the expulsion of the immature ovum. Autopsies on fœtuses during the Hamburg epidemic yielded nothing special in the way of macroscopical anatomical changes, excepting multiple ecchymoses of the pleura, the pericardium, the thyroid gland, the thymus gland, and the lungs. Bacteriologically the different organs and the contents of the ileum proved to be free from germs.

The puerperium was followed in a few cases by septic endometritis. The hemorrhagic affection of the uterus was associated in many cases with hemorrhages into the ovarian tissue, partly in the form of circumscribed hemorrhages, partly as extensive bloody infiltrations of the parenchyma. In one case the right ovary was changed into a tumor nearly as large as a fist, owing to a profuse hemorrhage, and the muscular uterine wall at the same time contained an extensive hæmatoma. Hemorrhages into the mucosa of the bladder were decidedly more frequent in women than in men.

In five instances a diphtheritic affection of the mucosa was discovered, partly in the form of a more superficial necrosis, partly with mortification of larger and deeper portions of the organ. In one case

there was a sloughing cystitis which had given rise to necrosis of nearly the whole of the mucous membrane and to a communication with the likewise diphtheritic vagina through a fistula the width of three fingers.

Serious disease of the *vagina* came comparatively often under observation. Two different forms could be distinguished, namely, a truly diphtheritic and an ulcerative form; the former, which was noted sixteen times by Fränkel, Simmonds, and Deycke, apparently had its seat of predilection around the cervix, from which it spread either diffusely over the entire vagina or irregularly in the shape of larger or smaller areas which were never sharply demarcated from the surrounding tissue. To the naked eye the vagina in such cases had a bluish-green discolored appearance and was covered here and there with thick dirty yellow crusts or with fetid shreds. The microscopical examination of this vaginal diphtheria showed that the affection was a diphtheria in the anatomical sense, *i.e.*, a direct mortification of the tissue. Bacterial stains disclosed besides cocci the presence of very numerous thin bacilli which occurred both on the surface and in the depth of the tissue.

In the second, ulcerative form, which was met with in eight instances, there were disseminated, flat tray-like ulcers varying in size, which were partly covered with eschars and were always sharply demarcated from the adjoining and little altered mucosa. In the only case of the kind that came under observation in the New General Hospital, in which the ulcers had a regular roundish oval form, microscopical examination with the well-known bacterial stains showed the presence in almost pure culture of a peculiar, rather long, straight bacillus with rounded ends and many vacuoles. Judging from the arrangement of these bacilli along the margins of the whole ulcer we may assume that they stand in etiological relation to the development of the ulcers.

In about twenty-four subjects who had died during the actual cholera attack our Hamburg prosectors examined also the *marrow of the long bones.* They found that the fatty marrow which filled the medullary cavity in a normal manner had without exception a raspberry color and the consistence of jelly; not rarely it contained some isolated focal and at times more diffuse hemorrhages. Microscopical studies of the minute processes underlying these changes could not be made, owing to the pressure of other work on hand.

Symptoms and Course.

Cholera indica is a disease at times ushered in by diarrhœa only, at times accompanied also by vomiting, the course of which presents the aspect of a severe specific intoxication, which frequently terminates in death. To arrive at a positive diagnosis the presence of the comma bacillus, discovered by Robert Koch, must be demonstrated in the discharges. Although Asiatic cholera cannot arise except through the action of the comma bacillus, the ingestion of these bacilli and their presence in the gastrointestinal canal, do not of necessity always cause cholera.

Cholera Infection without Marked Symptoms.

This absence of marked symptoms, which has lately been observed also in other infectious diseases, especially in diphtheria, for a long time led to the denial of the etiological relation of the comma bacillus to cholera. As previously mentioned, a few cases of autoinfection with the cholera bacillus in the laboratory were altogether without symptoms, while others presented only diarrhœal symptoms, but did not progress to a fatal termination. Nevertheless, a number of severe cases of choleraic disease have lately been observed after autoinfection with comma bacilli. These, and the death of Oergel from an attack of cholera acquired in the laboratory, have probably served to silence many objections.

At all events, the altogether negative experiments aroused great interest. Although a diminished virulence might perhaps be raised as an objection in these experiments carried on with cholera cultures from the laboratory, experience at Hamburg nevertheless proved that some individuals may, even in the midst of a severe epidemic, harbor cholera bacilli without contracting the disease. These observations were first made by my former assistant, Dr. Rumpel.

Among 60 cases, in which during the post-cholera epidemic of December and January, 1892-93, comma bacilli were found in the dejections, there were 19 persons, in whom disturbance of the general health was absent or hardly perceptible. Of these, 10 cases had diarrhœa for a few days, 6 for one day only, some of these had simply one watery passage, and 3 persons who harbored comma bacilli had formed movements. In 3 other cases of solid stools Dunbar demonstrated the presence of comma bacilli. These 6 patients, who were under observation for a long period, never complained of diarrhœa or other symptoms of illness at any time. Should these in-

vestigations be carried out among the entire population during an epidemic, we would probably find a large number of individuals who had received the poison of cholera without presenting any morbid symptoms. At all events we were again able, during the slight epidemic of 1893, to verify the presence of comma bacilli, with absence of any clinical evidences of disease in 9 out of 151 cases which came under observation. We must also take into consideration that only the smallest number of individuals suspected of infection are as a rule received at the hospital. Karlinsky was able in an epidemic in Arabia to demonstrate comma bacilli in the normal dejecta of two healthy individuals. According to Kaehler, 52 cases in which comma bacilli were found, but which presented no clinical symptoms of disease, were reported in Germany in the year 1894; during the same period there were 1,004 cases of cholera with 490 deaths. This number may have been so small, however, for the reason that the examinations were not made with sufficient care, because of the great distribution of the cases. Von Esmarch, in the village of Wehlau alone, found, aside from 8 typical cases of cholera (6 of them fatal), comma bacilli present for from six to nine days, without any other symptoms of disease, in 12 out of 35 persons kept under observation.

These experiments show that the intestine of man must contain certain antitoxins. The latter do not, however, seem unlimited. We find quite a number of interesting cases in the literature of cholera concerning persons who, having left the locality in which an epidemic raged seemingly in perfect health, gave expression to their joy in having escaped disaster by excesses of eating and drinking in the locality which they had reached. A severe attack of cholera coming on frequently within a few hours informed them and their neighbors of the dangerous visitor the emigrants had harbored. Many a person thus lost his life which had seemingly been saved.

This action of the cholera bacillus had been suspected even before its actual demonstration, for Lebert says: "There are probably many persons through whom the cholera germ passes without leaving any mark. In others its virulence is exhausted in an intestinal irritation of a few days' duration, but of temporary action only." These views have also led to the great importance attached as a general rule to diet during periods of cholera.

Choleraic Diarrhœa.

This is known to us partly as the true *first stage* of severe cholera, but much more frequently as the only symptom of an infection which has already taken place, no further development into the grave form

occurring. This choleraic diarrhœa is usually greatly disseminated at the time of an epidemic. In how many cases of infection a choleraic diarrhœa only occurs is difficult to say. Were we to base our conclusions solely upon the bacteriological findings in the hospital, we should obtain a percentage of seventeen. As, however, only a small percentage of the cases of choleraic diarrhœa comes under observation in the hospital, contrasted with the grave forms which are admitted in greater number, the percentage is probably much higher. We are forced to this conclusion also by the well-known fact that, since the appearance of Asiatic cholera in other countries than India, an extraordinary increase in cases of diarrhœa has been observed coincidently with those of true cholera, and for this increase we can find no other explanation than that of a genius epidemicus. Meanwhile individual epidemics seem to present great variations as regards the comparative frequency of the cases of diarrhœa and those of true cholera. But of whatever nature they actually are, it is advisable to regard these diarrhœal cases occurring in the course of an epidemic as cases of cholera, unless their innocence can be absolutely established by bacteriological evidence.

The diarrhœa of cholera is characterized by a greater or less number of watery muco-feculent and bile-stained passages. They usually come on during the night, frequently accompanied by gurgling and flatulence, as a rule without marked abdominal pain. With this the general health may be apparently unaffected at first, the appetite being normal. If the stools increase in number and diarrhœa continues, however, a coated tongue, a bad taste in the mouth, thirst, a feeling of weight in the region of the stomach, will not fail to appear. These symptoms may, however, as we have been taught by the interesting experiments of von Pettenkofer, be altogether absent, and after a few days the slight indisposition disappears without leaving a trace behind.

It is of the greatest interest to know within what time after the comma bacilli have been taken into the body the symptoms on the part of the intestinal canal will make their appearance. In settling this question, we must take into account the great number of cases of autoinfection. In von Pettenkofer's patients the diarrhœa appeared within forty-eight hours; in Emmerich, who incurred a complication by an error in diet, it came on in thirty-six hours after infection. In an experiment conducted by Metchnikoff, the initial diarrhœa appeared even more rapidly that this, that is to say, within twelve hours after the ingestion of the comma bacilli, although two days more passed before the true symptoms of cholerine developed. The duration of the diarrhœa is quite variable, as a rule from five to seven

days passing before those cases which exhibit a marked reaction again return to their normal condition. Comma bacilli have been found in the stools as late as the twelfth day. The experiments above mentioned lead to the conclusion that the onset of diarrhœa takes place about one to two days after infection has occurred, and that the disease sets in more rapidly only under certain conditions, and certainly never within from one to two hours after infection, as has so frequently been asserted.

The duration of this diarrhœa is also exceedingly variable. The trouble may, as above mentioned, cease within one or a few days, or may continue a much longer time; anorexia, restlessness, headache, diminution in the volume of urine, usually make their appearance. A dragging sensation in the calves of the legs, a tendency to perspire, and a rise of bodily temperature may also accompany these symptoms. In other cases the diarrhœa seemingly ceases and the stool again becomes normal; but should the patient only slightly neglect his previous circumspection in diet, the diarrhœa will start afresh, and, unless great care is taken, a grave form of choleraic disease may follow. Besides change of diet, carelessness in other matters, such as getting out of bed too early and the like, seems to exert an unfavorable influence. We must not, therefore, regard choleraic diarrhœa as a harmless disease. A fatal termination may occur in old and debilitated persons as well as in young children, and also in those in the midst of unfavorable surroundings, as for example in soldiers on a campaign, without the supervention of grave choleraic symptoms. The patient becomes weaker day by day, goes into collapse, and after a few days death takes place from exhaustion, although no distinct symptoms of cholera have appeared. These cases, from their nature, are deserving of special study.

Choleraic diarrhœa is characterized by the presence of comma bacilli in the stools. The latter were sometimes found to be present only one day in the epidemic at Hamburg; they were more frequently met with up to the eighth day of the disease. In two patients their presence could still be demonstrated on the twentieth day after the beginning of the illness. According to other observers there is no doubt that these microorganisms may retain their vitality in the intestine for a much longer time. The stools, which vary in number from one to twenty a day, do not possess any other marked characteristics besides the demonstrable presence of comma bacilli. They usually consist of the slightly yellowish contents of the small intestine. Typical rice-water stools very rarely occur in the early choleraic discharges. That this diarrhœa frequently merges into a prodromal stage of true cholera in some epidemics has already been

mentioned. In Hamburg, however, this was certainly not the rule. The greater number of cases of choleraic diarrhœa continued as such, and only a small percentage became worse. The stools in the latter event assume an appearance similar to rice water and with this, which is nearly always dependent on a greater amount of desquamated intestinal epithelium, the disease increases, with the addition of other symptoms. We then speak of

Cholerine.

This much more frequently appears as a distinct affection from the start rather than as a sequel of a simple diarrhœa of longer or shorter duration. Not uncommonly it is preceded by more or less severe general symptoms. We often note malaise, a feeling of languor, anorexia, perhaps nausea continuing for an indefinite period, and then suddenly frequent diarrhœal stools announce the true nature of the affection. These stools are yellow at first but soon assume the rice-water appearance. Although their number may not be especially large, vomiting now makes its appearance. At first food only is thrown up; then the vomited matter becomes yellowish-green, very thin, and has an exceedingly bitter taste. In only rare instances does it become altogether colorless, like whey or like rice-water. After vomiting has occurred a number of times, it may altogether cease, the diarrhœa, however, continuing. Anorexia, coated tongue, pain in the region of the stomach, excessive debility, buzzing in the ears, headache, and great thirst usually make their appearance with the increase of symptoms. Here and there an increase in the temperature of the body is noted, which cannot, however, be demonstrated by feeling the skin. The latter as a rule feels cool, the pulse is small, the secretion of urine is slight or altogether arrested; in the small quantity of urine albumin is found; the patient frequently complains of a dragging sensation in the calves of the legs, although spasmodic contractions are not necessarily present. If the symptoms increase, we then witness the typical picture of cholera. Frequently, however, the patient recovers from this attack of cholerine, but recovery does not always progress rapidly. In the first place, the diarrhœa may again make its appearance on the slightest provocation, or, on the other hand, a febrile or afebrile condition of general debility, with slight perspiration, coated tongue, and extreme thirst may set in. The debility and dulness of mind recall somewhat the sequelæ of cholera, to be described later, the so-called cholera typhoid of earlier writers. But, just as cholerine may gradually end in recovery, so may, on the other hand, the grave picture of true cholera develop

from it. This does not, however, appear to occur so frequently as was formerly supposed. While formerly the prodromal diarrhœas with their various accompanying symptoms were looked upon as the regular initiation to true cholera, it was found by the observations made during the recent epidemic at Hamburg that a transition from choleraic diarrhœa or cholerine to the algid stage of cholera only very rarely occurred. We may here, as Michael has emphasized, be dealing with differences in individual epidemics; or we may be permitted to believe that the early treatment of choleraic diarrhœa and cholerine may in this instance have had a favorable action. However this may be, the fact remains that in the greater number of the grave cases of cholera occurring in Hamburg the premonitory diarrhœa was absent, and we are therefore inclined to look on most cases of choleraic diarrhœa and cholerine as slight forms of true Asiatic cholera. Judging by our experiences in the epidemic of 1893, choleraic diarrhœa and cholerine probably compose one-half of all the cases of cholera; we must, however, emphasize once more the fact that these figures refer to the hospital material, in which of a certainty the greater number of cases of choleraic diarrhœa which occurred in the city are not included. It is therefore probable that the picture of cholera gravis is met with in much less than one-half of those attacked.

Cholera Gravis.

It has been generally accepted since Griesinger's time that prodromal symptoms precede this form for some time, often for several weeks, occasionally for from one to three days only. Similar observations were also made in Hamburg. These cases are, however, few in number compared with the much more numerous ones in which a suddenly appearing diarrhœa develops, within a very brief period, from one to six hours, into the worst form of cholera. The initial symptoms of the attack are exceedingly variable; sometimes nausea, restlessness, and chilly sensations precede the true attack; again, a violent diarrhœa comes on without any premonitory symptoms and is rapidly followed by nausea, retching, vertigo, etc. The diarrhœal stools are increased in number and assume the characteristic aspect, vomiting occurs, and in the course of half a day the grave picture of cholera is developed, accompanied by the typical manifestations of what the older authors called the asphyxial or algid stage of cholera.

We meet with individual cases, however, in which only very mild diarrhœa is present, and in which as a direct consequence vomiting and by far the most severe form of cholera intoxication develops with

the greatest rapidity. The course of the disease in these exceptional cases, in which the sufferers are suddenly obliged to leave their work on account of the occurrence of a few diarrhœal movements and are found within the period of half an hour quite cold and cyanotic, are scarcely to be explained in any other manner. Mistakes in diet also play a rôle in some cases; an especially peculiar predisposition is presented by the great number of laborers who are addicted to alcohol, are irregular in their meals, or are otherwise debilitated by disease. In the greater number of cases, however, no cause can be found for this malignant onset and course, for most of such cases observed in Hamburg occurred in men and women of robust constitutions, in whom the statement that they had lived a regular life could be accepted without a reserve. Evidence of the cessation or absence of diarrhœa in these cases was furnished also at the autopsy, firm fecal masses being found in the intestine.

Concerning the age of the patients, the greater number of cases occurred (we are here giving the statistics of the Hamburg epidemic) in patients between twenty and twenty-five years of age. But there were also many cases in infants under one year of age, a fact which to my mind has formerly not been sufficiently taken into consideration.

The beginning of the affection, leaving aside the prodromal diarrhœa, which was observed only in about one-fourth of the cases, is as a rule sudden. Following a feeling of general malaise with gurgling in the abdomen, the first diarrhœal passages make their appearance, frequently accompanied or followed even in this early stage by a dragging sensation in the thighs, an inclination to cold hands and feet, numbness of the limbs, and general restlessness. Other diarrhœal passages, sometimes very profuse, follow, and soon take on the characteristic aspect of rice-water stools; they are discharged painlessly, and may even be voided unconsciously. The whole aspect of the disease has by this time undergone a sudden change. After the appearance of excessive debility we note nausea and vertigo, buzzing in the ears, palpitation of the heart, anxiety, and oppression, but above all a feeling of pressure in the region of the heart and stomach. The patient's face becomes anxious and drawn, the skin loses its fulness, and takes on that glimmer of gray which early proclaims to the expert the approach of the algid stage.

Vomiting now usually comes on, at first of remnants of food, then of liquids which have generally been taken in large quantities, then of a bitter greenish or yellowish matter, and lastly of a flocculent liquid, resembling rice water, similar to the discharges from the bowels.

These evacuations by the mouth are frequently also accompanied

by the same from the bowels. To the distress and pain in the region of the stomach and heart are now added great thirst and internal heat. Some patients become anxious, restless, and excited, others fall into a certain apathy and somnolence, from which they only rouse themselves from time to time to ask for a drink. At this time an expression of pain may distort the face, indicating the spasmodic contraction of the muscles of the calf, or more rarely cramps of the muscles of the arms. The voice becomes hoarse, the skin, especially that of the extremities, is cool, the nose is cold and pointed, the forehead is covered with a cold sweat. The color of the skin becomes more gray, dark rings appear under the eyes, the hands, fingers, lips, and nails all take on a bluish tint. The temperature, as a rule, has already become subnormal, but the patient himself does not feel cold; he is continually complaining of heat and thirst. Drink is given him, but hardly has he swallowed the liquid when it is vomited. The vomiting is accompanied by a most distressing hiccough. The tongue, as a rule, is covered with a whitish coating, and in the course of time becomes dry and covered with a dirty dark-colored deposit; it is only with difficulty protruded by the patient. Beside the thirst and the convulsions which recur with extraordinary rapidity and frequency, many patients suffer greatly from a sort of precordial distress. Some, restless and complaining, throw themselves about, while others appear perfectly apathetic and somnolent. When they are spoken to, we can frequently demonstrate that their psychic functions are in a perfectly normal condition.

As already mentioned, the temperature usually becomes subnormal in this stage. The extremities, particularly the hands and feet, are the first to become cold, and from here the coldness spreads over the whole body. The lowering of temperature is, however, rarely as great as it seems. A temperature below 35° C. (95° F.) is not of frequent occurrence, but the moisture of the skin, which is at the same time present, gives the impression that it is much cooler. The pulse is usually weak, as a rule normal in frequency, rarely increased, and if so, hardly ever exceeding 100. Frequently it becomes weaker and weaker hour by hour. Respiration is as a rule increased. Even when no organic disease of the respiratory organs is present, the number of respirations is usually increased to 30 to 40 to the minute. The urine is commonly suppressed in this stage, or exceedingly scanty, although there are cases in which it is passed in large quantities. Thus I have observed a case, in which a patient, thirty-nine years of age voided 1,250 c.c. (about 40 oz.) of urine during the twenty-four hours preceding death in the algid stage; this urine contained 10 gm. N. and 2.075 gm. ammonia. The abdomen is flat-

tened and retracted; on percussion a slight dulness is obtained, and succussion of the fluid, with which the intestines are filled in spite of the great diarrhœa, may be felt when the integumental coverings are not too thick.

Hopeless as this picture seems, survival of this stage may nevertheless take place, the occurrence of later disturbances, however, not being excluded. The profuse diarrhœal discharges may diminish, sometimes while the vomiting still continues; at other times after its cessation the pulse becomes stronger, the color improves, and in the course of a few hours the grave attack seems to have passed over. Other cases with a constant increase of the grave symptoms end in death. The patients lie in bed, with symptoms of extreme exhaustion, with sunken cheeks and temples, and face and hands covered with a clammy sweat; the wrinkled, leaden-hued skin can be lifted up in great folds, the lips, fingers, and nails are of a bluish-violet color. Intelligence with all this may be fully maintained; as a rule, however, somnolence is present, interrupted now and again by an expression of anxiety and a sense of oppression. The voice becomes altogether lost, respiration becomes shallow, the pulse at the wrist disappears; now the carotid and femoral pulse also becomes indistinct, and the second sound of the heart cannot be heard. If a small artery is cut, blood does not flow; an incised vein also will allow only a little dark-colored blood to exude. In the mean while the thirst may continue, vomiting and diarrhœa (the intestinal discharges often being involuntary) may persist, and the muscular spasms frequently reach their greatest height at this time. With increasing coldness of the skin, the eyes gradually become staring, the lids are only partly closed, respiration becomes deep, sighing, or rattling, and death takes place with a total absence of consciousness. In this manner death may occur within a few hours even from the beginning of the attack, more frequently, however, in the course of the first or second day.

This typical picture of the algid or asphyxial stage of cholera has, it is true, undergone numerous changes during recent epidemics as the result of treatment. By means of hot baths, and above all, as a result of the subcutaneous or intravenous injection of a solution of common salt, a change bordering on the miraculous is obtained in these cases; the pulse becomes fuller, the cyanosis and gray discoloration of the skin disappear, the deeply sunken eyes come to life, respiration becomes deeper and regular, the spasmodic symptoms disappear, the face becomes flushed, the temperature rises to normal, and a gentle perspiration bathes the skin. Patients who had previously lain in an apathetic, comatose condition, giving no sign when called, paying no attention whatever even when the incision

was made in the skin over a vein, frequently wake as from a deep sleep during the injection of the salt solution, and the rough, hoarse voice of cholera becomes clear and intelligible. As by a conjurer's wand, the patient, sick unto death, has been seemingly raised to convalescence. This brilliant result, unfortunately, does not always continue; and in spite of perseverance in the employment of these injections, the algid stage again makes its appearance after a few hours, and cannot be dissipated for any length of time by our most persistent efforts. The patient dies after a somewhat protracted course of the cholera. Other cases seem to go on to recovery, but this recovery is not of any duration. The algid stage has disappeared, the pulse becomes full again, respiration is regular, the face is flushed, the voice has lost its hoarse tone; but yet the whole picture which the patient presents is peculiar. A condition is developed to which older authors have given the name of cholera typhoid, but which I should prefer to designate, in order to avoid misunderstanding, as coma following cholera, or the

Comatose Stage.

The patient, who perhaps seemed to be improving for a few days, suddenly falls into a condition of great debility and apathy. Now and then he complains of dulness and confusion of ideas, and of headache; frequently the latter can only be surmised, since the patient is lying in a kind of stupor, by the frequent moving of the hands to the head.

In other cases this stage almost immediately follows the algid stage of cholera; this has been frequently observed especially after the salt solution has been injected without benefit. If the temperature has returned to normal after the passage of the grave attack, or if it has even risen above normal for a short time, we now meet with a fall of temperature in severe cases; the proneness of the extremities to become cold, already present in the previous stage, again makes its appearance, cyanosis returns, the pulse being in the mean time full and strong. In contrast to the usually cool extremities, the head is hot, face and conjunctivæ are injected, and speech becomes indistinct; the patient hears with difficulty, and either becomes delirious (the delirium, however, is rarely active) or else he enters into an apathetic and somnolent condition. With this, the spasms of the muscles may continue or recur, and diarrhœa is usually present, though not of so frequent occurrence as before; these diarrhœas are, however, characterized by the fact that the vibrios of cholera are invariably found in the dejections, while the true secondary diarrhœas as a rule do not contain any cholera bacilli.

The presence of the latter for so long a period is the reason why I would refer this condition, previously regarded as a secondary affection, wholly to the cholera intoxication itself, or in greater part at least, and have spoken of it as a chronic cholera intoxication. Frequently the excretion of urine is now reduced or ceases altogether, and in any case, evacuation of the bladder rarely occurs voluntarily. The somnolence develops slowly into stupor and coma, and in this stage the patient dies. In other cases a picture resembling more the algid stage makes its appearance, and brings on the fatal issue by exhaustion.

Grave as some of these cases look, the patient may nevertheless recover occasionally. As a rule, improvement begins with the occurrence of a peculiar *exanthem*. Sometimes this makes its appearance in the form of an erythema, sometimes it resembles urticaria or an extensive roseola; frequently beginning on the hands, the eruption spreads over the arms, chest, back, and oftentimes over the whole body. As the maculæ become confluent, a general redness of the skin takes place, which can be traced only in a few localities to its origin from individual patches. This exanthem may be distinctly visible for one to three days, but fades as a rule soon after it has reached its full development. With the appearance of this eruption the somnolence and apathy may disappear, the symptoms of disturbance of the gastrointestinal canal may improve, and convalescence may slowly become established. This improvement is frequently deceptive, however. Heaviness of the head and somnolence recur, the alvine discharges again become more frequent, and perhaps also contain blood; vomiting may come on again, the pulse becomes more frequent and thready, the respiration is accompanied by tracheal râles, and death suddenly results without any further symptoms.

The issue is particularly unfavorable in those cases in which a subnormal temperature accompanies the other manifestations of a grave intoxication. Out of 183 carefully recorded cases of this kind, 165 died. This furnishes a mortality of 90 per cent.

Those cases run an essentially more favorable course in which, usually with less severe symptoms of mental disturbance, there is more or less fever. I leave out of consideration here, of course, all those cases in which complicating diseases are the cause of the elevated temperature. This fever may exist by itself alone, and is then considered as a fever of reaction and is so called. This may occasionally be observed, but it was not the rule in Hamburg. Usually a certain degree of apathy and somnolence accompanies the fever, in other cases slight muscular cramps may be felt, the patient complains of heaviness of the head and of malaise, speech is indis-

tinct, and disturbances on the part of the gastrointestinal canal also again manifest themselves through pain and tenderness of the abdomen together with diarrhœa. The less intense all these symptoms are the more favorable will be the course of the affection. Convalescence may suddenly occur with the appearance of the above-mentioned cholera exanthem, the headache, apathy, and somnolence are gone, the head is clear, the tongue becomes clean, appetite returns, and a recovery follows relatively rapidly. These lighter cases are usually, as we have said, accompanied by a rise in temperature, so that we may quite positively predict the course of the disease from the latter.

Inasmuch as this picture of a chronic intoxication nearly always follows the algid stage of cholera, it naturally makes its appearance more rarely as a sequel to cholerine, or even to a choleraic diarrhœa of longer duration, which has not been preceded by the so-called grave form of typical cholera.

Among the symptoms which accompany this intoxication a diminished excretion of urine should be mentioned. Coma has, however, been observed, even in those cases in which large quantities of urine have been voided. Furthermore, albuminuria must be reckoned as a frequent occurrence. Albumin may, however, be absent, or present in very slight amount. Griesinger was inclined to ascribe some of the cases called by him cholera typhoid to uræmia, on account of the frequent occurrence in them of this albuminuria. We shall have occasion to refer to these later on.

That this condition has no connection whatever with typhoid fever we need hardly attempt to demonstrate. It is true we meet with cases in which typhoid fever exists as a complication in cholera, but these cases do not differ either clinically or anatomically from ordinary typhoid fever; on the other hand, in the comatose conditions above referred to, designated by some as cholera typhoid, we do not find the enlarged spleen or the typhoid roseola, and fever is present only in very slight degree, being in the worst cases replaced by a subnormal temperature.

With this we have completed the description of the symptoms due to cholera infection and intoxication. We shall now pass on to the discussion of the individual symptoms of the disease, as regards their origin, etc. We will, however, defer the analysis of these for a time, and take up first a description of the true complications and sequelæ of Asiatic cholera.

Complications and Sequelæ.

Among the complications of cholera, we should mention, in the first instance, the affections of the respiratory organs. The presence of a *croupous pneumonia* contemporary with the algid stage of cholera was demonstrated by me, in the great epidemic of 1892, in a number of cases. These cases, it is true, did not show the characteristic fever, or at least in only isolated cases was there any rise of temperature; but the results of percussion and of auscultation, on the other hand, left no room for doubt as to the diagnosis, and furthermore, in a few cases the pneumonic sputum containing pneumococci was found. In other cases, circumscribed *catarrhal pneumonia*, in others hypostasis and *œdema of the lungs* were present as complications. Typical cases of cholera were observed a number of times in patients suffering from *pulmonary tuberculosis*. The existing affection in these cases was wholly uninfluenced by the cholera; the typical symptoms of cholerine, on the other hand, were usually but slightly marked. In one case of this kind the patient rapidly succumbed to exhaustion, notwithstanding the absence of the symptoms of typical cholera.

A number of patients suffered at the same time with *typhoid fever*, to the symptoms of which were superadded those of cholera. The roseola, enlarged spleen, and temperature curve did not undergo any change. On the other hand the aspect of the patient was less feverish, the face being rather of a grayish hue. The copious and occasionally rice-water discharges, containing comma bacilli, constituted the chief manifestation of the intercurrent cholera. In other cases there was no rise of temperature whatever, and the coexistence of typhoid fever with cholera was only discovered at the autopsy. No evidences of any marked reciprocal influence of one disease on the other could be detected.

A peculiar and grave complication of cholera is presented by the *diphtheritic* lesions in the intestines. These are capable of diagnosis only in those cases in which there is a discharge of blood and pus, of a bloody purulent, fetid stool. Frequently this grave intestinal affection is accompanied by meteorism, excessive tenderness, tenesmus, strangury, and vomiting. Its occurrence is not very rare. As a rule these cases end in death. If the bloody stool should occur but once, however, recovery is possible. Grave cases of intestinal diphtheria have frequently been noticed to follow large doses of calomel. That the latter was the cause seemed at least to be shown by the existence of the characteristic lesions in the kidneys.

Diphtheritic affections of the bladder and the female genitalia were

found as well as those of the intestinal canal. These also are frequently characterized by the presence of blood in the urine, etc. These diphtheritic processes, in addition to the danger inherent in the condition itself, expose the patient to the danger of a septic general infection arising from them secondarily. Should this occur during the typical algid stage, it may be accompanied by no fever whatever.

Hemorrhages from the female generative organs may also occur in the absence of any ulcerating diphtheritic affection, during the course of cholera, being due possibly to hemorrhagic infarction of the uterine mucosa. In this event, painful uterine colic accompanied by metrorrhagia will be noted. Seemingly as a consequence of this hemorrhagic infarction of the mucous membrane, perhaps also with the coöperation of a spasm of the uterine muscles due to the cholera intoxication, *abortions* or miscarriages occur with extraordinary frequency during an attack of cholera. In more than one-half of the cases pregnancy is interrupted, and the percentage of interruptions rises with the duration of pregnancy. The fœtus is usually stillborn. The prognosis as regards the mother also is not particularly favorable, as the number of deaths in such cases exceeds the average mortality of cholera. There are here added to the dangers of cholera those of a premature confinement under great difficulties. Nevertheless, very many of these lying-in women are saved.

It is generally supposed that convalescence and recovery are ushered in with certain *symptoms of reaction*. These, as Griesinger has justly remarked, frequently consist in nothing beyond the gradual disappearance of the grave symptoms which the patient presented. The profuse diarrhœa, when present, diminishes in frequency, and vomiting ceases; the radial pulse, which was absent or could hardly be felt, rapidly improves in quality and frequently takes on the character of a pulsus durus; the anæmic heart murmurs, which in many cases replaced the second sound, disappear, and the latter again becomes distinct, and the apex impulse can also again be felt. With this the cyanosis disappears, giving place frequently to a peculiar marble-like pallor for some time, the warmth of the skin returns, respiration becomes free, and the feeling of apprehension and oppression subsides. The bodily temperature rises, and not infrequently reaches 38° C. (100.4° F.). Partly in consequence of this, partly as a result of the numerous hot drinks swallowed, a profuse perspiration breaks out. The cramps will have already ceased, and the voice has now become clearer. The amount of urine passed at this time is, as a rule, still small, and it often remains scanty for a few days longer. The urine generally contains albumin. Congestion of the head and also some complaint of confusion of mind or headache are

quite frequently met with in this period. A relapse into the algid stage or into coma occasionally occurs even in this stage. Frequently all these symptoms fluctuate for a number of days or may be accompanied by various complications. If convalescence continues, the aspect of the patient improves day by day, the tongue becomes clean, the appetite returns, the strength slowly comes back, the secretion of the urine becomes more abundant, and the diarrhœa improves.

The general condition may essentially improve, and yet the number of diarrhœal stools may not markedly diminish. In all these cases, however, the rice-water character of the stools is changed to an appearance more nearly resembling bile. In some cases, the stools gradually decrease in number and become firmer in consistence, the excretion of urine becomes more copious, a warm perspiration bathes the patient, occasionally an exanthem appears, and in a few days the patient is well.

This was, however, not the most frequent course of the disease in the Hamburg epidemic. Much more frequently secondary disturbances followed, among which an *intestinal catarrh* may be mentioned. After the general condition had quite markedly improved and more infrequent and firmer discharges had taken the place of the repeated liquid stools, diarrhœa would suddenly reappear, without any other symptoms. It is natural to suspect, in such a case, a recurrent attack of cholera. This thought seems to be justified the more, as we are aware that true choleraic diarrhœa containing comma bacilli occasionally does make its appearance, in the absence of grave constitutional symptoms. We also know, of course, that a perfect and typical relapse may follow the first attack of cholera after apparent recovery has occurred. This was especially noted in persons who took no sort of care of themselves after improvement or apparent recovery. The relapse, so far as we can judge from the small number of observations, is by no means marked by a favorable course, a fact which is of special interest in its bearing upon the theory of immunization.

In the hospital, and with proper treatment, relapses of this kind certainly are the exceptions, and the diarrhœa which may follow the first attack of cholera, after a short interval, when the general condition is good, does not seem to be caused by the presence of comma bacilli in the intestines. The absence of comma bacilli has at least been demonstrated in a large number of cases which were studied especially to determine this point.

When we compare these diarrhœal stools with those of cholera, it is interesting to note that in the diarrhœas of the secondary period the stools are tinged with bile and have a fecal odor. Occasionally, even in this form of diarrhœa, the presence of comma bacilli can be

demonstrated in the stools. This coincidence could be found, however, only in isolated cases, and as a rule only during beginning convalescence, so that in general the faculty of the comma bacilli for further development and growth may be said to end with the appearance of normal intestinal discharges. If then the cause of this secondary diarrhœa cannot be found in the presence of the comma bacilli in the intestine, and if judging from the general well-being of the patient it is hardly probable that the strong and accelerated peristalsis is due to the belated action of toxins, it is permissible to regard the lesion of the intestine as the probable cause of the affection. This theory of the etiological significance of the intestinal lesions, which as a rule are easily healed without any complications, is strengthened by the course of these secondary diarrhœas. For, in spite of the great number of the stools, a number which may even exceed that met with during the attack of cholera, the prognosis, in the absence of complications, cannot be said to be unfavorable.

In one case, in which during a grave attack of cholera lasting eight days, about thirty-two rice-water evacuations took place, there followed, after a pause of four days, during which time all the symptoms of cholera had entirely disappeared, a second period of diarrhœal stools, which continued for twenty-four days and aggregated more than one hundred passages. Occasionally the number of the latter reached eight to ten in twenty-four hours. The amount of each evacuation was variable, although by no means small and always exceeding that of the discharges during the attack of cholera. At the same time the general condition remained good, it is true, and the appetite was excellent. Day by day the diarrhœal stools of this second period were examined for comma bacilli, always, however, without result. The case ended in recovery.

It is certainly remarkable that in these cases of diarrhœa all other dangerous symptoms remain absent, if the patient is kept in bed, a distinct hint that other causative factors than the loss of fluids are responsible for the grave general condition in the symptom complex of cholera indica as well as in that of cholera nostras.

In a few cases a longer duration of the secondary diarrhœas was observed, especially when the patient was careless of himself, and marked debility, emaciation, inability to work, paroxysms of anxiety, and oppressed breathing were not wanting. In these cases, which were not of frequent occurrence, there was usually also anorexia, but as a rule all ended in recovery, even though continuing sometimes for months. Only in exceptional cases were psychic disturbances of a melancholic character noted as sequelæ.

Neurasthenic conditions have come under my notice more fre-

quently during recent years, the origin of them having been referred by the patients to a previous attack of cholera. These, however, as well as the irritability of the gastrointestinal canal and the inclination to diarrhœa may have been due to the excessive fear which some patients had experienced for weeks.

Of special interest among the sequelæ of cholera have always been the *disturbances of the function of the kidneys*. Griesinger attributes a portion of the so-called cholera typhoid to uræmia, particularly those cases in which the urinary secretion is altogether suppressed, or soon ceases, or becomes scanty, and the small amount which is passed contains a large quantity of albumin. We shall have occasion to enter more minutely into these views, in discussing individual symptoms. Although I am in general of the opinion that these cases may be explained in a different manner, the fact of the disturbance of the urinary secretion in the cases reported by Griesinger admits of no doubt. Albumin, in larger or smaller quantity, frequently accompanied by finely granular cylindrical casts, is found not only in these cases, but quite generally after an attack of cholera, thus affording a proof that the kidneys are particularly involved in this affection. This disturbance, however, runs a relatively rapid course as a rule, and does not furnish an absolutely certain proof that a typical nephritis belongs to the frequently occurring sequelæ of cholera. I have, however, devoted very special attention to this point, and have minutely examined all those patients who returned to the hospital again after recovery from an attack of cholera, in order to determine whether there was any permanent affection of the kidneys. In only one case, however, one which I observed in the private practice of Dr. Voigt, did such a connection seem probable. All the other examinations gave negative results.

The patient mentioned above, forty-two years of age, had passed through a short but typical attack of cholera early in September, recovering from which he returned to his business. About fourteen days later, after he had resumed his ordinary occupations, he suddenly became ill with pain in the loins, restlessness, malaise, vomiting, and diarrhœa, but without fever. Examination of the urine, which was voided in moderate amount, revealed a specific gravity of 1.022 to 1.025, albumin, and many cylindrical casts. There was a hard pulse. Under a milk diet and a light sudorific treatment perfect recovery followed.

This has so far remained the only case in which a nephritis following an attack of cholera could be suspected. Meanwhile this case is not altogether free from objections, as it might be possible that recovery from the renal lesion caused by the cholera process had been

retarded by the early rising of the patient. Other affections of the kidneys following cholera, especially cases of contracted kidney, could not be detected in any case in spite of a careful search.

It may certainly be supposed that the symptoms of contracted kidneys may appear later in a patient who has passed through an attack of cholera; but we must not forget, taking into consideration E. Fränkel's and my own findings, that we may be dealing with another affection of the kidneys which is independent of cholera, and which may have existed prior to the attack of this disease.

Individual Symptoms.

The Intestinal Tract.

Cholera is a disease which finds its way into the economy through the intestinal canal, and which becomes first localized in the latter, principally in the small intestine.

While the stomach exerts a defensive power against the invasion of cholera bacilli, a power of defence which is probably related to the secretion of the acid gastric juice, the small intestine furnishes a locality in which the invading microorganisms can display their activity. The results which make themselves felt after the invasion are naturally dependent partly on the virulence of the invading germs of infection, or on their number, and partly on the toxins produced by them. At least we may explain in this manner without any difficulty some differences which have occurred following an invasion of larger or smaller quantities of cholera bacilli. There must, however, also take place a more or less rapid increase of bacilli in the small intestine in some individuals. For it is impossible that the large quantity of cholera bacilli which are found within the small intestine and in the lumen of the gut could have all been introduced through the mouth. This increase is an extraordinarily varied one, so that we are compelled to ascribe to the human organism certain defensive powers against the invading carriers of disease. One part of this defensive power is certainly of a chemical nature, and is probably based on the formation of toxins. Another part may be of a motor nature, the intestine endeavoring by increased peristaltic action to eliminate the unpleasant and noxious visitor.

We will study first simple choleraic diarrhœa, the intensity of which, as we have seen from the clinical description, is extraordinarily variable. During the course of this diarrhœa the other functions of the body may be well maintained. Thus the appetite is usually not at first affected, the tongue retains its normal red color, and thirst, in spite of frequent stools, is in the beginning hardly noticeable. Fre-

quently the evacuations from the bowels are preceded and accompanied by gurgling and rumbling noises in the abdomen, at other times they occur without any premonitory symptoms at all. The number of stools in choleraic diarrhœa is extraordinarily variable. Sometimes there is only one diarrhœal stool containing comma bacilli each day, in other cases ten and even more fluid passages occur in the twenty-four hours; the patient, however, presenting no especial morbid symptoms beyond the diarrhœa. In some the diarrhœa lasts only one or a few days, in others its duration is prolonged over many days, it may even recur from time to time during several weeks. Accompanying true choleraic diarrhœa, we naturally also meet, in the course of an epidemic, with many other forms of diarrhœa which do not owe their origin to an infection. These cases may be differentiated from choleraic diarrhœa by the absence of comma bacilli. In individual cases certain psychic disturbances may be regarded as the real cause of these diarrhœas; in others the same causes exist which produce diarrhœa at other times, and their action is increased by the excitement which agitates the community in times of cholera. Simple choleraic diarrhœa is rarely accompanied by grave symptoms of disease or warnings of the same; at the most we note, as in other forms of diarrhœa, diminished excretion or suppression of urine, albuminuria, more rarely dragging sensations in the calves of the legs, and hoarseness, evidences that the seemingly innocent diarrhœa has a more or less serious condition back of it.

With the removal of the invading bacilli from the intestine the cholera infection certainly comes to an end in a very great number of cases. Only in debilitated individuals the simplest form of diarrhœa may lead to death, in which case the dejections retain their feculent character perfectly. In other cases choleraic diarrhœa is seemingly the introduction to a grave form of the disease. In this case, the removal of the comma bacilli does not seem sufficient to enable the resisting power of the organism to protect against any further invasion by the germs of infection.

In other cases directly following the diarrhœa there occurs a more severe picture, that of *cholerine*. This affection is frequently directly developed with the first diarrhœal discharges, or else follows it so rapidly that we cannot speak of a real separation into two stages. It is even possible for the various symptoms of intoxication, such as restlessness, headache, malaise, disturbance of the appetite, and coated tongue, to precede the true attack for hours. Then only do the dejections occur, at first yellowish-brown, later of a deeper yellow color. At the same time vomiting usually takes place. The impression is given almost as though the organism had hesitated for a time

to make sufficient use of peristalsis, and in the mean time had afforded an opportunity for the toxins of the cholera bacilli to become absorbed and exert their general poisonous action. Among these we might mention besides a feeling of fulness and tension in the abdomen, together with anorexia and a coated tongue, also nausea and vomiting. In true cholerine the latter does not occur very often. It may be repeated several times, but usually ceases in a short time. Alt has recently expressed the view, and tried to support it by experimental investigation, that a portion of the cholera toxins is excreted by the stomach. If this is also true of cholerine, we may look upon the degree of intoxication in the latter as being still a low one. For the termination of cholerine, as of cholera nostras, which owes its origin to a similar parasitic infection, is as a rule in recovery. It is true that in this affection some signs of a grave cholera intoxication may also make their appearance. Thus we often note a diminution of the urinary secretion accompanied by the presence of albumin in the scanty secretion, and headache, vertigo, buzzing in the ears, and general debility may exist for days after cholerine has run its course; the functions of the stomach may also be disturbed for a long time. In this manner perfect convalescence after an attack of cholerine is always a matter of some time. The duration of true cholerine, according to the observations made in Hamburg during the year 1893, was from one to four days. In isolated cases the attack does not even last one day. When the comma bacilli are evacuated by the intestine, the affection may speedily be recovered from. That the cholera bacilli may leave the intestine very quickly can be seen from the results of some very careful observations of cases of cholerine made in the year 1893. Comma bacilli were found in:

2 cases	on the 1st day only.	3 cases	as late as the 6th day.
10 "	as late as the 2d day.	1 case, "	" 8th "
6 "	" " 3d "	1 " "	" 9th "
4 "	" " 4th "	2 cases "	" 10th "
3 "	" " 5th "	2 " "	" 12th "

That the comma bacilli may remain in the intestine for a much longer time, and that their presence may be demonstrated in the stools, has already been mentioned. In true cholerine this condition does not seem to be the rule. In accord with this statement is the observation that typical cholerine, such as is seen in hospital cases, leads rarely to the severe form of true cholera, but usually runs its course as a disease *sui generis*, in which death occurs as a rule only from complications. It may be urged against this view that cholerine in the event of grave infection leads so rapidly to true cholera that these cases seldom come under observation in the hospital. The

fact nevertheless remains that we do meet with a large number of cases of cholerine which do not pass into cholera gravis. In this connection it is worthy of note that when an entire family is attacked, one member may perhaps be taken ill only with diarrhœa, another with cholerine, and one or more of the others will have true cholera. A similar observation has been made by Lebert in his report of cholera at Zurich.

The evacuations of a true choleraic attack, in contrast with those of the conditions just considered, have the appearance which has given rise to the term rice-water discharges. While it cannot be denied that yellowish-colored dejections frequently precede these evacuations, yet the peculiar qualities of these is so early manifested that they may be designated as characteristic of true cholera. These dejections give out a peculiar insipid odor, such as also often rises from the opened peritoneal cavity of a body dead from cholera. Under the microscope these stools are found to contain, aside from the cholera bacilli which are generally present in large quantities in each cover-glass preparation, various other microorganisms of different and varying forms, but especially great quantities of intestinal epithelium and masses of detritus with lymphoid cells.

This *epithelial desquamation*, as has been already mentioned in the section on pathology, is a constantly recurring anatomical finding at the autopsies of persons dead with cholera. The mucous membrane of the intestine is denuded of its epithelium for some distance. This condition also seems to me to be the cause of the grave cholera infection. We are aware that the intestinal epithelium presents the most potent protection against the intestinal contents, which are frequently of no indifferent nature. If the former becomes necrosed by the action of the toxins, the mucosa with its extraordinarily rich network of vessels becomes exposed, and an essentially grave process is started from that instant. The vital processes in the intestinal canal, which are characterized by the elective ability of the epithelium to absorb and excrete, simply give place to the mechanical laws of diffusion, such as are active in every serous membrane lacking epithelium. The toxins of the cholera bacilli enter the mucosa in large quantities, the cholera bacilli themselves preceding or following, and now a greater distention of the blood-vessels and lymphatics of the whole injured small intestine takes place, which leads to that rose-colored or purplish tint which is recognized as characteristic even after death. Griesinger rightly emphasizes the fact that this stasis involves mainly, and often only, the small intestines, and not the other parts of the portal system, that the liver and the spleen as a rule do not present any symptoms of venous engorgement, and that

accordingly certain causes must be present in the small intestine which influence this congestion independently of the occurrences in the general circulation. This cause Griesinger believed to have found in the desiccation of the blood circulating in the small intestine, which he argued would greatly thicken it immediately and render it slow of movement. If this view of Griesinger were the true one, the presence of the same pinkish or purplish tint would not be found in the small intestine in those cases of death from cholera in which an infusion of many litres of normal salt solution had been practised, and in which cases therefore no question of a thickening of the blood could be raised. It has not, however, been possible to demonstrate any difference in this relation. We are therefore compelled to refer the great distention of the vessels to the direct influence of the bacilli or of their toxins. That the great distention of the smaller and smallest arterioles may also be a factor in the production of venous stasis seems to be plausible when we remember the decrease in the velocity of the blood current and the transudation which takes place into the intestine.

The occurrence of an active congestion of this sort was noted by Virchow in his examination of the mucous membrane, and especially of its glandular apparatus, in cases of cholera. A slowing of the circulation might, however, also obtain, if the toxins of cholera, as is probably the case, exert a paralyzing influence on the muscular coat of the vessels. If this be true, we have yet to explain only the occurrence of transudation into the intestine, which we must assume from the copious evacuations, in the absence of the ingestion of fluids. Griesinger attempts to explain this by assuming the presence of poisons in the blood, which lead to transudation into the intestine in a manner similar to that which occurs when tartar emetic is injected into the blood. We cannot reject these considerations as devoid of a certain basis of probability, but another explanation may, in my opinion, be found. We may look upon the contents of the body and of the intestine as two fluids of different densities, which after the removal of the epithelium of the small intestine are separated from one another by a membrane. Of these two solutions, that inside the body, namely, in the blood and lymphatic vessels, undoubtedly is under a higher pressure than that within the intestine. It therefore seems quite natural that fluids transude into the intestinal lumen from the vessels, while the toxins of cholera and other products of disintegration diffuse themselves from within the intestine into the body. This process is also demonstrated by the presence in large amount in the urine of grave cholera cases of an indigo-forming substance. The rice-water matter in the intestine is, however, passed

on from time to time by peristalsis, and as the cholera bacilli are frequently left behind, this process of diffusion may again repeat itself. The quantity of fluid diffused from the inside of the body into the intestinal lumen is, however, by no means as large as is frequently supposed. To obtain a few quarts of the intestinal contents, I was obliged to collect the stools of many cholera patients, as well the matter filling the intestines post mortem.

That the presence of the comma bacilli within the small intestine plays an important rôle in the grave attacks of cholera is with certainty established from what has been said, and from the finding of the cholera bacilli in the stools. Examination for cholera bacilli, in seventy cases of severe cholera, yielded the following results: Comma bacilli were found in:

13 cases,	5 fatal,	on the 1st day only.				
8 "	5 "	as late as the	2d day.			
12 "	4 "	" "	3d "			
7 "	2 "	" "	4th "			
7 "	6 "	" "	5th "			
2 "	2 "	" "	6th "			
5 "	2 "	" "	7th "			
4 "	2 "	" "	8th "			
1 "	1 "	" "	9th "			
3 cases,	1 fatal,	as late as the	10th day.			
1* "	0 "	" "	11th "			
2 "	2 "	" "	13th "			
1 "	1 "	" "	14th "			
1 "	0 "	" "	15th "			
2 "	0 "	" "	16th "			
1 "	0 "	" "	17th "			
1 "	0 "	" "	19th "			
1 "	1 "	" "	24th "			

* In this case the bacilli were found in formed stools.

If, after deducting the fatal cases, we compare this table with that of cholerine on a preceding page, we find that in cholerine, in 53 per cent., the cholera bacilli were present in the stools during three days only, and in 17 per cent. for a longer period, at the longest up to twelve days. On the other hand, in true cholera the presence of comma bacilli in the stools terminated only in 27 per cent. of the cases by the end of the third day, while in 63 per cent. the comma bacilli were still passed in the stools after the third day, and in the different cases from that up to the twenty-fourth day. These figures prove to a certainty that the grave aspect of cholera is conjoined with a longer stay of the cholera bacilli in the intestinal canal. It strikes me as being of especial importance that in the stools in what was formerly called cholera typhoid, which were nearly always present although not so frequent, comma bacilli could always be demonstrated. This occurred with perfect regularity, in contradistinction to the negative results obtained with the same regularity in the light secondary forms of diarrhœa.

As the cholera bacilli rapidly disappear on perfect recovery from true cholera, their continual presence in the grave form of the disease must be regarded as of some importance. Basing my views on this

result, as well as on a clinical and pathologico-anatomical study, I am compelled to look on the comatose condition following cholera, the old cholera typhoid, as a sort of chronic cholera intoxication.

We cannot, it is true, determine the number of comma bacilli in the intestine from the mere presence of them in the discharges. In those cases in which comma bacilli were found in the dejections ten to fourteen days after the attack, their number seems to have been very small, while we frequently meet with very large numbers in the more severe and recent cases; however, some of these seem to be destroyed in the deeper parts of the intestine, as the entire number of comma bacilli contained in the fresh preparation cannot always be developed in the cultures.

Occasionally the bacteriological examination will give a negative result on the first day, and a positive one only on the second or third day, a knowledge of which fact should lead us to employ great care in basing a diagnosis upon such an examination.

In a typical attack of cholera the stools early take on a rice-water-like appearance as already mentioned, and they may also retain this character during the whole course of cholera. At times, however, an admixture of blood is early discovered in the dejections. If the amount of blood remains moderate its presence in the stools is not a directly dangerous symptom, but its appearance at all events leads us to suspect the presence of hemorrhagic infarctions in the intestinal wall, but especially in the follicles. Should the blood in the dejections increase, or should the latter take on a sanguino-purulent character accompanied by a fetid cadaveric odor, a *diphtheritic* affection of the wall of the intestine may be suspected, such as has already been described in the section on pathological anatomy. These changes naturally carry with them an especially unfavorable prognosis.

A tentative prognosis may also be based upon other appearances of the stool. Moderately frequent watery stools, which still retain some color, are of a good prognosis, but more unfavorable are the typical rice-water evacuations, especially if they are very copious. On the other hand, infrequent evacuations, while the intestines still contain much fecal matter, are of unfavorable import, especially if the other symptoms continue; a complete cessation of the dejections, under these conditions, is decidedly unfavorable. Should the stools again resume a biliary tint, this may be looked upon in general as a favorable symptom.

The Stomach.

In cases of simple choleraic diarrhœa the functions of the stomach may remain undisturbed. The tongue and taste are normal, the appetite is not diminished, there are no eructations from the stomach, and no sensation of pressure.

In cholerine the stomach is usually more deeply involved. In this case anorexia and a sensation of pressure over the stomach may precede for some time the real attack. After this *vomiting* occurs, either accompanying or following quickly the diarrhœal evacuations. The vomited matters consist at first only of remnants of food, later these will probably be mixed with bile, the taste of which the patient describes as exceedingly bitter. Finally there may be vomited a whey-like or rice-water-like fluid. This, however, occurs much more rarely in cholerine than in the severe form of cholera. We have learned above that the stomach in very few exceptional cases presents the same grave changes that are seen in the small intestine, namely, extensive necrosis and hemorrhagic infarctions of the mucous membrane. In cases of this kind the affection of the stomach may be directly responsible for the vomiting. In the greater number of cases, however, this is met with when no grave lesions of the stomach are present. The stomach empties itself with surprising ease and rapidity. Should the vomiting continue, a distressing singultus may follow. Disgust for food and nausea will usually not remain absent when the vomiting is of longer duration. The precordial distress which is present in a severe case and the feeling of pressure over the stomach cannot probably be referred to the stomach. At all events, the vomiting should not be looked upon as a *signum mali ominis;* the impression it gives is rather that the patients must feel easier after a thorough emptying of the stomach. Griesinger thinks that a long continuance of the attack of vomiting should be looked on rather as a favorable than as an unfavorable sign. This naturally does not apply to the vomiting of blood, which probably makes its appearance only in cases of grave infarction of the gastric or intestinal mucous membrane.

The vomited matter has frequently been examined chemically. The presence of urea and ammonia in it has given rise to the idea that a vicarious excretion of the products of metabolism normally evacuated through the kidneys was performed by the stomach. I have, however, frequently met with similar findings of urea and ammonia in cases of simple nervous vomiting, so that the results of these examinations of the vomited matter have not demonstrated

specific functional disturbances which can be ascribed to cholera alone. An experiment undertaken by Alt in 1892 is of great interest. Alt believes that an excretion of the cholera poison is accomplished by the mucous membrane of the stomach, much in the same manner as has also been demonstrated in the case of morphine. He also claims that he has extracted the cholera poison from the vomited matter. These results, of which we of course need corroboration, are very interesting and significant. They would explain the improved condition of the patient after the vomiting, and enable us to understand more readily the fact that many patients clamor for liquids in spite of the vomiting which is sure to follow.

The vomiting which comes on in the later stages of cholera, the stadium comatosum, has been frequently explained as of uræmic nature. We shall have to examine this question more in detail in the course of our discussion of the renal functions. It is quite likely, however, that we also have to deal here with similar causes and changes as in the earlier stages of cholera.

The Circulatory System and the Temperature.

Symptoms on the part of the circulatory system and of the heat regulators are constant in cholera. The simple form of cholerine presents the latter in a slight degree only. First, palpitation of the heart, a general beating of the arteries, and a feeling of apprehension usually make their appearance. Very soon, however, a weakening of the circulation is added, particularly in a grave attack of cholera. Frequently this is preceded at first by an increase of cardiac action, which may attain 90 to 120 beats to the minute. Then the heart beat grows less strong and the arterial pulse becomes remarkably weaker. This may be seen most distinctly in the radial pulse, which becomes thready and may disappear altogether when the arm is raised. The carotid pulse also becomes weaker. The same may be said of the second sound of the heart. It was noticed in the early epidemics, especially by Dieffenbach, that the arteries which had been exposed by an incision were narrow and small, that they very rarely emitted a full stream of bright-red blood on puncture, but as a rule bled very little or not at all, and when isolated were totally empty of blood. These symptoms may probably be explained solely by a continually increasing debility of the heart's action. This debility leads to a marked decrease of pressure throughout the whole arterial system, of the greater as well as of the lesser circulation, and following both, the temperature of the surface seems to decrease. At the same time, an accumulation of blood takes place in the venous system. This disturbance of the circulation keeps pace with the intensity of

the intoxication, so that the condition of the radial pulse becomes of great importance for the diagnosis and prognosis of cholera gravis. When the first grave attack of cholera has passed, the circulatory disturbances also disappear rapidly as a rule; the pulse rises in strength and again becomes bounding, being sometimes accelerated, at other times retarded, and occasionally hard, in isolated instances dicrotic; these variations in the character of the pulse, however, have no positive prognostic significance.

In proportion as the blood in the arterial system is reduced in volume the venous system becomes more and more engorged, in consequence of the diminished *vis a tergo* of the after-pressing capillary blood and the weakened cardiac action. Even from the veins, when incised, the blood does not usually flow freely, and these vessels may in the algid stage of cholera be exposed and traced as in the dead body. The venous system of the abdomen seems moreover to contain most of the blood; the great veins in the neighborhood of the heart are usually filled with dark blood of the color of tar.

The diminution or absence of the arterial circulation in the skin leads to two symptoms that are probably also met with similarly in other circulatory disturbances, namely, a cooling of the body and cyanosis. The latter is, however, only rarely found so intense and so distinctly marked in any other disease as in cholera. This stage of cholera is designated the *algid stage*. The patient is cold to the touch, a cold sweat covers the skin and makes the sensation of cold appear yet greater than it is in reality. The temperature nevertheless is usually distinctly lowered at this time. This is more marked at first in the peripheral portions, so that the axillary temperature will be found relatively lower than the rectal. A marked difference between the inside of the body and the periphery does not, however, as a rule long exist. The rectal temperature also decreases one to two degrees Centigrade (two to three and a half degrees Fahrenheit), and later this fall is probably increased. Naturally, the radiation of heat towards the periphery is, as Bärensprung has also emphasized, markedly diminished. That the peripheral parts, however, participate chiefly in the general lowering of the temperature, that the feet, the hands, the legs, and the arms are especially cold to the touch, is once more mentioned here for the sake of completeness. The nose and forehead likewise are exceedingly cold. The patients themselves, on the other hand, complain of a feeling of heat and even of burning. It was therefore believed that the coldness of the surface was coincident with a rise of the internal temperature. But although there are exceptional and usually mild cases of cholera in which the body temperature is

elevated, there is always in the algid stage a lowering of the temperature.

The causes for these disturbances of the circulation and of heat regulation have been widely discussed. The great amount of water lost by the body and the resulting inspissation of the blood, and also the cooling of the blood in the peripheral portions, have been discussed as factors leading to this result. Biernacki's researches, by which he demonstrated an increase not only of the leucocytes but also of the red blood corpuscles in the blood of cholera sufferers, are in accord with this theory.

These factors are not sufficient, however, to explain the extreme degree of cardiac failure. Griesinger says that it is not altogether impossible, indeed it is probable, that this is due to a primary action of the poison on both the intestine and the heart, an action which cannot be questioned in the case of many other poisons. It is, however, much more plausible, he continues, to assume that it is a sort of sympathetic action proceeding from the intestine, a view that is supported by the analogy of the depressed cardiac action following an acute obstipation which appears now and then in isolated cases of severe poisoning. The peculiar effect upon the circulation of various grave disorders of the abdominal organs, and particularly of the peritoneum, lends further probability to this theory. Whether this action is dependent on nervous influences, or on absorption of noxious substances from the intestinal canal, must at present still remain doubtful. Although nervous influences may also play a rôle, a poisonous action of the cholera bacilli must under all circumstances be looked upon as proven, since Pfeiffer was able with a very small quantity of perfectly fresh cultures, about eighteen hours old, to produce the disease by intraperitoneal infection in guinea-pigs. The disease was demonstrated one and a half to two hours after infection, the animals remained quietly huddled together, the temperature of the intestine was lowered two to three degrees Centigrade, there were fibrillary twitchings of the muscles, and death occurred with a still greater fall of temperature, which often went down to 30° C. (86° F.) and below. As there was no question in this infection of any intestinal disease, diarrhœa, loss of fluids from the body, etc., and as the vibrios were as a rule, or at least frequently, absent from the peritoneal cavity, the symptom complex could be referred only to the action of some poison. The great similarity of these symptoms with those of the algid stage of cholera is, however, seen at once. Although the latter becomes thus somewhat clearer to our mind, with its peculiar symptoms, we are still for the present unable to find any similar explanation for the comatose stage, the so-called cholera typhoid.

That comma bacilli were always found in this stage in our experiments at Hamburg, either in the dejections or in the intestinal canal post mortem, has been mentioned above. If we should now assume a poisonous action of the comma bacilli, we should have to admit its presence also in the comatose stage. It is, however, surprising that the toxin should show its action in two very dissimilar ways, at one time in the algid stage and then again in the comatose stage. It may be now taken for granted that the end of the algid stage is determined by the fact that the amount of toxin circulating in the blood has diminished, or that the body has become accustomed to the action of the poison, either because this latter is elaborated in less concentrated form or because some substances are generated which antidote the action of the toxins. In this manner we should be able to explain one part of the so-called cholera typhoid, especially if we are compelled to deny uræmia as a cause, as we shall explain more at length below. This chronic intoxication must certainly be increased still more by another condition. The epithelium of the intestinal canal in these grave cases is nearly entirely exfoliated, and the noxious matters contained in the intestinal contents become diffused through the blood-vessels and the lymphatic system, in consequence of the great injury to the mucous membrane. That a great number of substances are present in the interior of the intestinal canal, whose entrance in the body must conduce to grave disturbances, need hardly be emphasized. Thus the chronic intoxication, or the cholera typhoid, may very probably be due to an accumulation of various poisons in the body, the condition being aggravated by the fact that the changes in the kidneys in all probability increase the difficulty of the excretion of these substances. In the same way may be explained the appearance, rare it is true, of coma in cholera nostras.

The Respiratory and Vocal Organs.

Disturbances of *respiration* play only a secondary rôle in the true symptom complex of cholera. In a severe attack of cholera the patients frequently complain, it is true, of a feeling of constriction and oppression of the chest, and also of difficulty in respiration. An increase in the rapidity of respiration is usually not present, however. Percussion and auscultation demonstrate, in the absence of these complications already mentioned, a normal condition. Notwithstanding this, the patient's complaints may rest on a true basis. Should the propulsive power of the heart become paralyzed, its effects will be manifested in the pulmonary circulation by a slower current of blood in the lungs. The small amount of blood in the pulmonary arteries also leads to the result that the blood becomes

more and more deficient in oxygen, a condition which is, as a rule, met with subjectively and objectively in all similar affections. Whether with this there is also a disturbance of the oxygenation, due to the toxins of cholera, cannot be positively stated at the present time. The view of Emmerich, that the formation of nitrites and methæmoglobinuria accompany cholera, has certainly not been confirmed by other observers. The dark blood of cholera may be converted, by shaking with air, into a perfectly bright-red condition, and the typical bands of methæmoglobin are not present in the spectrum of the blood in cholera.

The complications of cholera with diseases of the respiratory organs have already been discussed. That they are of a secondary nature, and not connected with a primary pulmonary localization of the cholera bacilli, has been sufficiently demonstrated by former observers.

We will mention here only the *vox cholerica*. We have already demonstrated in the section on pathological anatomy that quite marked degenerative changes may occur in the laryngeal muscles, a fact which was demonstrated by the studies which Boltz conducted in the New General Hospital at Hamburg in 1892. These processes might easily be thought to be in relation with the hoarse voice met with in cholera. We were able, however, by intravenous and subcutaneous injections in the algid stage, to cause the disappearance of this hoarse voice, together with the other grave symptoms. We are therefore obliged to assume that the disturbances of the circulation in the muscular tissue have produced the peculiar debility and the paresis and paralysis of the vocal cords observed by Matterstock.

The Kidneys.

The participation of the kidneys in the cholera process has for a long time been the subject of scientific interest. The generally total *suppression of urine* at the very beginning of cholera, the subsequent appearance of albumin and cylindrical casts in the urine, and the similarity of the secondary cholera symptoms to those of uræmia, have again and again drawn attention to the kidneys. We need only mention the studies of Griesinger and Lebert in this field. In the first stage of cholera the symptoms of an involvement of the kidneys are, it is true, overshadowed by the grave general symptoms. The only symptom pointing to an affection of the kidneys is anuria, which is nearly always met with in typical cases of any severity whatever. It would nevertheless be venturesome to diagnose from this single symptom a true disease of the kidneys, as it is probably sufficiently known that anuria lasting one to two days may be present

in other diseases which are accompanied by a profuse diarrhœa. If therefore a greater importance is ascribed to the anuria of cholera, this is only because, as the case goes on, still other symptoms make their appearance which point to the kidneys.

That anuria, however, belongs to the clinically important symptoms of Asiatic cholera may be seen by the following:

In about 3,000 papers on the cholera question which I have examined, I find mentioned in only 698 cases that no anuria was present during the first few days of the disease. The amount of urine voided, it is true, was often small; in one case it amounted to only 20 c.c., or 5 drachms. Out of these 698 cases, 33 died—thus furnishing a mortality of 4.7 per cent.

It may be said that some of these numerous cases which are marked as not having suffered from anuria were not cases of cholera at all, that at the height of the epidemic an examination for the presence of comma bacilli was not made in all cases. Several mild cases of cholera are, however, recorded in which a seemingly normal excretion of urine was present in spite of the presence of comma bacilli.

A number of such cases were observed in the great August–September epidemic, and more exact observations were also made in the small epidemic of December and January. In thirty-two cases, we find three in which comma bacilli were present, which were and remained free from anuria; in three cases the comma bacilli made their appearance in the stools during the course of the anuria, the excretion of urine not presenting any change, and eight cases showed anuria on the first day only of the disease, the excretion of urine being perfectly sufficient during the remainder of the attack. Of the latter cases, only two showed albumin, the rest, as well as those mentioned above, were free from albumin. All these cases ended in recovery.

Opposed to these cases, which presented a seemingly normal or nearly normal excretion of urine, anuria was present in 1,031 cases, 590 of which, therefore 57.2 per cent., resulted in death. If we, however, take into consideration those cases in which anuria existed longer than two days, we find 85 deaths in 268 cases. This will give us a mortality of 31.5 per cent., while all the cases of cholera which lived longer than the first two days furnish us with only 22.5 per cent. of fatal cases.

We ought, therefore, to look upon the excretion of urine as a symptom of great prognostic significance in cholera, in so far as a normal or nearly normal excretion of urine during the first or second day of the disease allows of a comparatively favorable prognosis.

This symptom is naturally connected with the changes which the kidneys undergo very early, perhaps a few hours after the commence-

ment of cholera, and which have already been described in the section on pathological anatomy. A severe involvement of the kidneys, at all events, does not exclude recovery. In two cases in which for a long time the stools were semisolid, the first secretion of urine was noted only in the twelfth and fifteenth day respectively, although it should not be forgotten that small quantities of urine were doubtless voided with the stools. Anuria of three to seven days' duration is nothing unusual in cases of cholera, in those which end in recovery as well as in those which terminate fatally. Those cases, however, in which anuria disappears early have a more favorable prognosis, although there is by no means a fixed ratio between anuria and a fatal issue. The proportion of those who die while the urinary secretion is copious to those who die with symptoms of anuria or a very marked decrease of urine is about as 4 : 6. The amount of urine first passed is usually small, in some cases amounting to only 20 or 30 c.c. for example, in others a much larger amount (400 or 500 c.c.) is passed; but the voiding of a large quantity of urine at one time after an anuria lasting several days is the exception. In one case, however, an excretion of 3,500 c.c. (7 pints) of urine was observed on the third day after an anuria lasting two days. The specific gravity was 1.020, and this urine as well as that voided on the following days contained albumin and many hyaline casts.

The urine passed first is turbid, as a rule, and of a yellow to a brownish color, but the specific gravity is not always very high. Not infrequently it is higher in the urine first secreted than in that of the following day. Specific gravities of 1.020 or 1.015 are not altogether exceptional. The presence of albumin in the urine during the first few days after the attack is nearly the rule in cholera. In one case with a favorable termination, albumin was present as late as the fourteenth day of the disease, anuria having persisted for three days. The specific gravity in this case fell in the course of eleven days from 1.025 to 1.008. The amount of urine rose from 1,300 to 2,200 c.c. (40 to 70 ounces).

Microscopical examination shows the presence of hyaline or granular epithelial casts, rarely mixed with blood corpuscles. No constant difference is noted in the number of casts between the cases which run a favorable and those which run an unfavorable course.

Although the grave involvement of the kidneys cannot therefore be looked upon as the true cause of an unfavorable issue in the later stages of cholera, the idea is nevertheless justified that it plays an important part in the course of the disease, and that the comatose stage especially may be referred to it. It seemed desirable, therefore, to observe the conditions under which excretion of urine and the

nitrogenous end-products of metabolism occurred in cases of coma following cholera, and to compare the results with similar comatose processes in other affections. As regards the urinary secretion, we may mention the findings in the case of two patients with cholera who, in spite of a copious secretion of urine, became comatose and remained so to the end.

S. A.——, 40 Years Old, Admitted September 17th, 1892.

	Temperature. Centigrade.	Amount of urine, expressed in cubic centimetres.	
1st day	35.1–36.2	Anuria.	....
2d "	35.5–37.2	Anuria.	....
3d "	35.8–36.9	Anuria.	....
4th "	36.0–37.0	Anuria.	....
5th "	36.0–37.0	100	Albumin.
6th "	36.0–37.0	200	Albumin.
7th "	36.0–37.0	500	Albumin.
8th "	35.6–36.1	1,200	Albumin.
9th "	35.4–36.5	1,000	Albumin.
10th "	35.5–38.4	550	Albumin.
11th "	35.2–37.2	850	Albumin.
12th "	35.4–37.5	500	Albumin.
13th "	35.6	Died.	

S. F.——, 20 Years Old, Admitted August 26th, 1892.

	Temperature. Centigrade.	Amount of urine, expressed in cubic centimetres.
1st day...	36.8	Anuria.
2d "	35.8–36	Anuria.
3d "	Normal.	Scanty.
4th "	Normal.	Anuria.
5th "	Normal.	Scanty.
6th " ...	Normal.	Anuria.
7th "	36.7–37.2	400
8th "	37.0–38.3	2,000
9th "	37.9–38.6	2,800
10th "	37.5	Died.

In each of these cases coma occurred on the seventh day.

In these two fatal cases, therefore, coma made its appearance while urine was being secreted and continued while the secretion was abundant.

In the following case death also took place in coma, while there was still a copious secretion of urine.

Adlang, 34 years old, peddler. The patient became ill during the night of August 29th to 30th with diarrhœa, vomiting, and cramps in the calves of the legs. He was taken to the New General Hospital, and improved slightly up to September 1st. On September 2d the diarrhœal stools again became more frequent, and in the course of a few days vomiting set in with lowering of the temperature to 35° C. (95° F.). On September 8th somnolence occurred, and on the 9th death followed. The excretion of urine during this time was: 5th to 6th September, 650 c.c.; 6th to 7th September, 1,000 c.c.; 7th to 8th September, 950 c.c.; 8th to 9th September, 1,250 c.c.

In regard to this case we may add that the kidneys were examined post mortem and extreme degenerative changes of the secreting epithelium were found.

We see, therefore, that the continued excretion of urine does not

prevent the occurrence of coma in cholera. It might nevertheless still be possible that in spite of the large secretion of urine at times a retention of the nitrogenous end-products of metabolism might occur. For the solution of this question we have undertaken, in a large number of cholera cases, the quantitative analysis of the total daily quantity of nitrogen excreted, according to Kjeldahl's method. We show here the figures obtained in four cases, giving first for comparison two cases of contracted kidneys accompanied by uræmia.

Uræmia.

Mr. K——, 78 years old, admitted February 22d, 1893. Contracted kidneys, hypertrophy of the heart, œdema of the legs, and ascites; slight uræmic convulsions, coma. Died March 9th, 1893.

Mrs. W——, 43 years old, admitted January 8th, 1893. Contracted kidney, uræmic convulsions, neuroretinitis, albuminuria, œdema of the legs, ascites, exudation into the pleural cavities. Died January 19th, 1893.

Mr. K——				Mrs. W——		
Date.	Quantity of urine.	Specific gravity.	Amount of nitrogen.	Date.	Quantity of urine.	Amount of nitrogen.
February 26th.	1,100	1.017	7.986	January 9th..	850	4.165
" 27th.	600	1.020	8.444	" 10th.	300	1.596
" 28th.	700	1.020	4.212	" 11th.	450	.....
March 1st.....	700	1.017	7.154	" 12th.	800	.....
" 2d.	600	1.019	6.384	" 13th.	900	.....
" 3d.	500	1.021	5.740	" 14th.	800	.....
" 4th	400	1.022	5.096	" 15th.	375	2.117
" 5th	500	1.022	6.650	" 16th.	Anuria.	.....
" 6th	400	1.023	5.208	" 17th.	400	2.52
" 7th	300	1.023	3.570	" 18th.	20	1.24
" 8th	300	1.025	3.780			
" 9th	350	1.025	4.508	The vomited matter contained:		
				January 12th.	.....	0.182
				" 13th.	.....	0.28
				" 14th.	.....	0.29
				The pleural effusion contained:		
				January 9th..	.....	1.52
				" 10th	.....	1.86

Cholera.

Friedrich W——, 35 years old, admitted December 16th, 1892. A typical case of cholera with profuse diarrhœa, great cyanosis, small pulse, vox cholerica, comma bacilli in the stools.

Michael W——, 32 years old, laborer, admitted December 25th,

1892. Copious diarrhœa, cyanosis, cold extremities, cramps in the calves of the legs, vox cholerica, comma bacilli in the stools.

FRIEDRICH W——

Date.	Quantity of urine.	Specific gravity.	Amount of nitrogen.
December 16th.	Anuria.	....	....
" 17th.	300	....	....
" 18th.	900	1.019	8.432
" 19th.	1,500	1.015	9.06
" 20th.	2,000	1.012	9.70
" 21st.	650	1.015	3.82
" 22d..	600	1.022	7.484
" 23d..	400	1.022	4.816
		1.013	

From December 22d the patient gradually recovered.

MICHAEL W——

Date.	Quantity of urine.	Specific gravity.	Amount of nitrogen.
The first 9 days.	Anuria.		
December 30th.	400	1.006	3.248
" 31st.	1,000	1.006	9.1
January 1st....	2,000	1.009	12.04
" 2d	2,700	1.009	10.58
" 3d	3,000	1.014	12.12
" 4th....	1,200	1.005	6.72
" 5th....	2,400	1.006	10.416
" 6th....	2,500	1.006	8.5
" 7th....	900	1.009	3.186
" 8th....	700	1.010	2.744
" 9th....	1,400	1.010	8.92

From January 4th gradual recovery took place.

Coma following Cholera.

B——, 26 years old, admitted January 31st, 1893. Diarrhœa, stools containing comma bacilli, vomiting, cramps in the calves of the legs, cyanosis, hoarse voice. On February 7th slight somnolence appeared and deepened to stupor on the following day. The man died on February 10th, 1893.

W. R——, 29 years old, admitted December 18th, 1892. Diarrhœa, stools containing comma bacilli, vomiting, cramps in the calves of the legs, cyanosis, hoarseness, somnolence on January 2d. Pneumonia appeared and the patient died on January 3d, 1893.

B——

Date.	Quantity of urine.	Total amount of nitrogen.
January 31st..	Anuria.	.....
February 1st..	Anuria.	.....
" 2d..	200	.....
" 3d..	Anuria.	.....
" 4th.	250	.....
" 5th.	Anuria.	.....
" 6th..	Anuria.	.....
" 7th..	1,600	7.168
" 8th..	1,800	8.316
" 9th..	1,100	4.70
" 10th*	950	4.498

*From the bladder.

W. R——

Date.	Quantity of urine.	Total amount of nitrogen.
December 23d.	1,200	.....
" 24th	750	8.59
" 25th	2,500	19.75
" 26th	1,300	14.43
" 27th	1,100	11.8
" 28th	Anuria.	.....
" 29th	880	9.85
" 30th	700	6.468
" 31st	1,500	11.85
January 1st...	1,000	10.22
" 2d...	1,400	18.63

The vomited fluid, although repeatedly examined, did not yield any nitrogen.

These examinations all demonstrate that there is no direct relation between the occurrence of coma following cholera, or of recovery, and the amount of the nitrogenous end-products of metabolism excreted. The examinations undertaken in the clinic of F. von Koranyi in Budapest by von Terray, Vas, and Géza Gara also failed to demonstrate any such connection. We may say, therefore, that no definite influence can be attributed to the excretion of the nitrogenous end-products of metabolism during the secondary disease processes. For if fatal coma occurs in spite of a normal excretion of urea, and if in other cases a copious excretion of nitrogen exists together with a bad general condition and improvement only begins many days later, then surely an insufficient excretion of nitrogenous substances in the urine cannot be the cause of the coma or of similar grave conditions, especially as the gravity of the symptom complex in nephritis and cardiac insufficiency is as a rule in inverse ratio to the amount of urea excreted.

We must now conclude that the coma of uræmia as well as that of cholera is caused not so much by the nitrogenous end-products of metabolism as by substances of some other nature, concerning the chemistry of which we are, however, as yet entirely ignorant. We are thus forced back to a study of the clinical symptoms. In this respect it is undoubtedly of importance to know that in a few cases of choleraic coma the fundus of the eye has been examined, and the absence of any of the changes accompanying nephritis has been noticed. Furthermore, I do not consider it unimportant to point out that the pupils were usually found contracted in the coma of cholera, while in uræmic conditions the pupil is usually dilated. The regular and considerable presence in the urine of indoxylsulphuric-acid compounds in cases of cholera has no complete analogue in nephritis. Another differential point to remember is the condition of the pulse. This is not always the same, however, in cholera, as we meet at times with a hard pulse, at times with a small pulse. Now it might seem that the first would accompany coma, especially in those cases in which there is an insufficient secretion of urine, but from a study of a somewhat large number of histories in regard to this point no definite and certain results have been obtained. At times a very small pulse is found together with total anuria, at times a hard and full pulse in cases in which there is an abundant secretion of urine. The same may be said of albuminuria. This undoubtedly points to the fact that the condition of the pulse, in the whole course of cholera, is dependent on altogether different factors, entirely independent of the more or less disturbed functions of the kidneys.

If we rapidly review the results derived from the comparative study of coma following cholera and of that following uræmia, we find the following:

During the first stage of cholera we find in the greater number of patients a decrease in the excretion of urine, consisting in anuria of one or two days' duration, followed by albuminuria. Those cases of cholera which run their course without any essential disturbance of the urinary secretion, as a rule have a favorable prognosis. In the second stage of cholera, the clinical participation of the kidneys is demonstrated in part by anuria or a decreased secretion of urine, in part by albuminuria. The involvement of the kidneys is in so far of importance in the estimation of individual cases as, *cæteris paribus*, a fair secretion of urine permits of a favorable prognosis. Nevertheless death may take place in coma, and in the absence of any other complications, in spite of a copious flow of urine as well as of a sufficient excretion of the nitrogenous end-products of metabolism. On the other hand, an anuria and albuminuria of long duration occurring after a first attack of cholera may end in recovery. We are not in a position, therefore, to look upon the involvement of the kidneys as the direct cause of an unfavorable issue in cholera, but think that we may regard it as not the cause but rather the expression, as a rule, of a more or less severe choleraic affection.

The results of the anatomical researches in thirty-nine cases, which E. Fränkel and myself have reported, and which have already been minutely described in the section on pathological anatomy, are very easily reconciled with these clinical findings. The question is only, How are these findings of the choleraic kidney to be explained? Cohnheim and more recently von Leyden are of the opinon that the changes in the kidneys are to be referred to the circulatory disturbances accompanying cholera, and especially to the arterial anæmia of these organs. The other view, supported by Klebs and later by Fränkel and myself, returns to the action of the cholera virus and looks upon the kidney affection as due to the action of a toxic substance, through whose influence a direct injury is done to the renal epithelium, which is especially sensitive also to the action of many other poisons. This view is furthermore corroborated by the fact that similar changes in the epithelium of the convoluted tubules are found in other infectious diseases, which are not accompanied by a loss of the fluids of the body, such, for example, as pneumonia and typhoid fever.

Whether this peculiar affection of the epithelium of the kidney possibly reduces the excretion of the cholera toxins, and in this manner retards the purification of the body, is an idea which ought

certainly to be taken into consideration, perhaps may be solved by later experimental investigations.

We have yet to mention briefly the presence of a substance in the urine which has hardly received the attention it deserves. This substance is *indican*, which is not absent, in all probability, in any grave case of cholera. Whether its presence is to be referred only to the fact that the mucous membrane devoid of its epithelium absorbs indican in larger quantity from the intestine, or whether still other factors enter into its presence, needs further study.

Finally, the condition of the bladder is to be mentioned. We should be exceedingly cautious in diagnosing anuria without an examination of the bladder. In cholera, as well as in many other infectious diseases, it may happen that retention of urine occurs. Here it is our duty, not only to make a proper diagnosis, but also to relieve the patient from unnecessary pain.

The Nervous System.

Robert Tytler, who in 1817 first met with cholera in Jessora, was from the first inclined to look upon it as a form of poisoning. Since then attention has been again and again drawn to the similarity of the symptom complex to that of some cases of poisoning. We will only mention poisoning by arsenic in this relation. This similarity has received an explanation in recent times by the discovery of the toxic qualities of the cholera bacillus. Animals poisoned with this toxin, according to R. Pfeiffer, become dull and weak, sit huddled together, and have after a time, together with other symptoms, fibrillar muscular twitchings. Muscular debility and muscular spasms are also in human cholera the first and most essential symptoms on the part of the nervous system. Now and then the patients suddenly collapse as if paralyzed, or they drag themselves laboriously to a nearby house, to be taken from here to the hospital. This extreme debility, which very rarely attacks the cerebral functions so early in other affections, may appear at a time when other symptoms, such as diarrhœa or vomiting, are still absent, or when diarrhœa is present in only a slight degree. In the second stage of the disease, dragging sensations and particularly cramps in the calves of the legs usually make their appearance. The thighs, the upper extremities, the muscles of the chest, abdomen, back, and face may also be attacked by spasms. As a rule, the true seizure of tonic spasms lasts for only a short time and is particularly distressing by reason of its great painfulness. However, even when these cramps occur only in paroxysms the whole muscular tissue of the patient is usually in a state of rigidity, which is also shown post mortem by the peculiar position of the limbs.

This symptom was formerly referred to the draining of fluids from the muscular tissue and to the disturbed conditions of metabolism. The intravenous infusions of salt solution, however, produce little or no amelioration in this, so that we are obliged to impute the condition mainly to the intoxication.

The prostration of the whole nervous system may also be referred to the same cause, and likewise the coma, as has been already discussed; the symptoms of anxiety and precordial distress, however, are referable to the insufficient oxidation of the blood and the excess of carbonic acid present in it.

The *mind* in the algid stage is but little affected in the majority of cases. A certain apathy is indeed frequently present, probably caused by the prostration and by the subjective symptoms; but when we converse with these patients, even the dangerously ill, their clearness of thought is often surprising, and in marked contrast with the physical signs of approaching death. Other patients throw themselves about in despair, until death overtakes them, with a horrible clearness of mind, fighting with all the force of their will against illness and death.

An altogether different picture is presented in the comatose conditions, as they are developed during the attack with more or less rapidity. Here the involvement of the mind comes to the fore, somnolence, frequently combined with slight delirium, stupor, and coma make their appearance. The etiology of this condition has already been discussed. Now that the uræmic nature of its origin can no longer be upheld, and now that the constant presence of comma bacilli in these cases forces us to the belief that the same cause is always at work, we are naturally led to refer the condition to an intoxication, in which the cholera vibrios are concerned. Together with this, the absorption of other poisons present in the intestinal canal must likewise be taken into consideration, especially as comatose conditions have also been observed in cholera nostras.

Trophic Disturbances.

Among the trophic disturbances we may mention first the peculiar change of the skin in cholera patients. If a fold of the skin is pinched up, it remains for some time in this position. This symptom conjoined with the cold and moist condition and the bluish-gray hue of the skin is nearly characteristic of cholera. The origin of this symptom may be in part referred to the loss of fluids from the body. Perhaps also an insufficiency of oxygenated blood has placed the skin and the subcutaneous connective tissue in a condition approaching mortification. This is corroborated by the fact that grave necrotic

processes in the form of brownish and blackish spots are seen on the cornea and the conjunctiva, more rarely on the skin, which, if the patient recovers, are thrown off and leave an ulceration behind.

After the true attack has run its course, peculiar forms of eruption are frequently noticed on the skin, which have been called the *cholera exanthem.* These are usually met with in cases of moderate and extreme severity, especially in conjunction with a chronic intoxication, so that they are seen more frequently in the second rather than during the first week of the disease. They usually begin in the form of circumscribed patches of erythema, of some size, more rarely in the form of a roseola. As they enlarge they may cover the greater surface of the body, and thus present an appearance almost resembling erysipelas. The color, however, is usually of a lighter red. If these patches remain circumscribed, urticaria-like forms may arise. These eruptions seem also to have been observed in the form of a scarlatina or variola exanthem (Griesinger). These erythema-like eruptions as a rule begin on the arms, less frequently on the face, and then spread to the trunk. The coming out of the eruption, which is said to vary in different epidemics, is usually accompanied by an improvement in the general condition, so that it may be regarded prognostically as a favorable sign. Numerous cases go on directly to recovery after the appearance of the eruption. It may, however, also happen that the improvement accompanying the exanthem is only a temporary one, and that in some cases the picture of a grave intoxication returns after a short period of improvement and leads to a fatal issue.

The trophic disturbances which attack the female genitalia and which influence unfavorably the course of pregnancy in cholera have already been minutely detailed above, so that we may pass them over here without discussion. That various kinds of metastases and infarctions occur as sequelæ of secondary infections in the course of cholera (also from intravenous infusions of non-sterilized salt solutions) need only be mentioned.

It is not possible to say whether the parotitis described by Rayen and Müller has the same etiology, or occurs only as a chance coincidence. True pyæmic processes were hardly ever observed by me in the Hamburg epidemic. The dry gangrene of the fingers or toes, described by Griesinger as occurring very rarely, would doubtless be an interesting complication. Wall writes from India that in severe cases of cholera the scrotum, and in rare cases the penis also, become gangrenous. My assistant Reiche has described a case of symmetrical gangrene of the skin of the margin of both ears occurring in the Hamburg epidemic.

Duration and Mortality.

Prominent authorities in cholera epidemics assert that each individual epidemic bears its special characteristic, which is due to the fact that now one, now another group of symptoms stands out most prominently. Thus it is said that the symptoms relating to the gastrointestinal canal, such as diarrhœa, vomiting, anxiety, etc., are at one time very marked, at another time they fall into the background and are replaced by the picture of grave intoxication. We have already drawn attention to individual differences of this kind in a previous section. We should perhaps also mention here that choleraic diarrhœa may, in children or debilitated persons or individuals otherwise ill, lead to death, without the occurrence of any noticeable cholera symptoms. Death takes place here with symptoms of exhaustion. Nevertheless very typical cases of cholerine and cholera gravis are also met with in children.

The duration of an attack of cholera is a relatively short one. A simple choleraic diarrhœa may come to an end in one day and even with one loose passage. Nevertheless, the cholera bacilli may still be present in the intestine for a number of days, and the fact that any injury, above all an error in diet, may during this time not only lead to a fresh choleraic diarrhœa, but even to the grave picture of cholera, is undoubtedly to be explained in this way. As a rule, however, choleraic diarrhœa lasts only a few days, although complications with other diseases may prolong its existence. Thus a case of true choleraic diarrhœa was observed to last a period of twenty-four days in the year 1893.

True cholerine also is of short duration. The main symptoms usually disappear in one or two days, within which period, however, debilitated individuals, and especially atrophic children, may succumb. In only rare cases is cholerine much prolonged, and in such cases of long course as a rule it passes over into the true cholera diarrhœa; very rarely indeed it develops into a cholera gravis. Nevertheless cases of cholerine were observed in the Hamburg epidemic in which convalescence did not set in before the end of two weeks.

Cholera gravis generally lasts a much longer period of time. Here we meet with premonitory diarrhœas, which were present in one-fourth of the cases during 1893, and which in individual patients ran on for fourteen days. The true attack is naturally short. Some patients recover in spite of the most pronounced cholera symptoms within a few hours. This is, however, the exception. A duration

for a period of two to three days is much more frequent. In only a few patients does the true attack of cholera last longer, and when it does it is then apt to pass directly into coma. The number of cases of coma is small for the reason that many deaths occur during the severe primary attack. Some patients die within a few hours, others within the first few days. The epidemics do not, however, seem to be altogether alike in this respect. Griesinger believes that one-half of all the deaths take place within the first forty-eight hours and the great majority of these during the course of the first day. Out of nearly five thousand deaths which occurred in the first epidemic of Paris, the duration is said to have been on the average sixty-one hours, but at the height of the epidemic only forty-three hours. With this fact, Griesinger says, agrees the experience that death occurs more frequently during the primary attack in the beginning of the epidemic, but towards its end more frequently in the stage of coma. Similar observations were also made in the great epidemic at Hamburg in 1892, while the after-epidemics in Hamburg in the winter of 1892–93 and in the autumn of 1893 presented an altogether different condition. During the great epidemic, and especially in its beginning, most of the deaths occurred during the primary attack (nearly one-third of the deaths took place in the first two days of the disease). In 1893 less than one-half of the deaths occurred during the first three days, the majority occurring after that date as late as up to the twenty-fourth day. This postponement of death may, it is true, have been due in part also to the intravenous infusions practised. With the reduced mortality of the primary attack brought about by this means, the number of deaths in coma increased. Rarely is the grave attack of cholera followed by a relapse, but the possibility of this should also be taken into consideration.

The mortality of cholera may be studied more minutely on the basis of a bacteriological examination. The mortality as a rule is about fifty per cent., and occasionally one of sixty per cent. has been reported. This difference depends partly upon whether the diarrhœas occurring at this time are counted as cholera or not. As, however, many more than was formerly supposed live through a cholera infection manifested by the occurrence of one or two diarrhœal stools, the assumption of an average mortality of fifty per cent. is certainly too great. Undoubted differences, however, exist between individual epidemics, for even in the course of the same epidemic a marked variation in the number of deaths had been noted, as we have mentioned already in speaking of the epidemic at Paris. An essential difference is certainly to be recorded in Hamburg between the grave epidemic of the year 1892 and the slighter one of 1893. The epidemic of 1892

began with a mortality nearly reaching 60 per cent. in the first fourteen days, declined in the following fourteen days to 50 per cent., and ended with a mortality of 20 to 30 per cent. The cholera epidemic of the winter of 1892–93 presented a mortality of about 20 per cent. On the other hand, the lesser cholera epidemic of the year 1893 reached a mortality, in 151 bacteriologically examined cases of true cholera, of only 46, or 30.5 per cent.

If we were to calculate the mortality of cholera according to these bacteriological findings, the total mortality would fall very far short of that formerly assumed. The mortality in the small epidemic of Bürgeln near Marburg, in the year 1894, was still less; here, only 4 patients out of 17, making 23.5 per cent., died. The mortality in eastern Prussia the same year was, however, in the vicinity of 50 per cent.

We are compelled, from these instances, to regard it as positively settled that the mortality of cholera is essentially variable, not alone in individual epidemics, but also in different localities, a view which has been corroborated by the studies on cholera of Hirsch, who was able, after comparing a large number of epidemics, to demonstrate a fluctuation in the mortality of twenty-two to sixty-six per cent. These differences have already been attributed to certain variations of the virus in the section on etiology, whether this difference is caused by varying degrees of virulence which the bacilli possess in different localities, or whether it depends upon the quantity of germs entering the body. In support of the latter view, Rumpel thought to make use of the experience of the water-supply commission of Hamburg. The favorable or unfavorable soil, which the imported vibrios would find, was supposed to show itself in the more or less vigorous growth of the microorganisms. The development of the symptom complex is, however, not directly dependent on the quantity of the vibrios present, as von Pettenkofer and Emmerich have demonstrated. The age of the patient is also of some influence upon the mortality figures. Thus, children are particularly threatened in the first two years of life, especially in the first year, while persons between five and twenty-five years of age present a marked resistance to the disease and a low mortality. From the age of twenty-five the susceptibility and mortality both increase largely, and become very high after the age of fifty, yet patients over seventy years of age may survive an attack of the disease. The manner of living and the condition of health in which an individual is at the time of the attack naturally influence the course of the latter to some extent. Sickly and debilitated individuals more readily succumb; this may in part explain the enormous mortality often met with in armies in the field and in camp.

Persons addicted to the abuse of alcoholic beverages are also in particular danger. These all are factors which play a prominent rôle in conjunction with the form and gravity of the infection. In typical cholera gravis, the mortality is, on the average, probably greater than fifty per cent. A marked influence on the mortality has also been ascribed to the time at which patients come under treatment. This, however, was not demonstrated in the measure expected during the great epidemic in Hamburg. Notwithstanding the greater distance which the main cholera districts were removed from the New General Hospital in comparison to the old one, the mortality in the first was if anything rather smaller than that in the old hospital. It is, however, naturally desirable, from a humane point of view, that the seriously ill should receive proper assistance as soon as possible.

Diagnosis.

The diagnosis of cholera indica is by no means so simple as was formerly, or even after Koch's discovery of the cholera bacillus, supposed by many.

The symptom complex in individual cases of cholera is, it is true, so characteristic that few other diseases can be mistaken for it. The fact, however, that other causes may also produce a similar symptom complex admonishes us to great care in the diagnosis, and all the more as the positive presence of true cholera should lead to incisive prophylactic and hygienic measures.

Cholera is, of course, to be diagnosed, and rightly, when very many cases presenting the typical picture of cholera have occurred, and among them a great number of deaths, and when anatomical changes characteristic of cholera indica have been found post mortem, and when finally some other cause, especially an intoxication, cannot be found. Even here, however, a bacteriological corroboration will be more than welcome.

The diagnosis becomes essentially more difficult when the cases are isolated, especially when only a single case presenting the symptoms of cholera has occurred. In this case the possibility of a cholera infection is as earnestly to be considered as that of poisoning. In this respect, poisoning by arsenic must above all be considered when the symptoms are those of the algid stage. Poisoning with solanine and colchicine is said to produce symptoms similar to those of Asiatic cholera. The greatest similarity is, however, probably produced by mushroom poisoning, especially as cyanosis of the skin is also present here; delirium is, however, absent in cholera. Grave cases of poisoning by sausage and by fish may frequently be differentiated

from cholera by the absence of the peculiar color of the skin. This, however, is certainly as little true for all the stages as for all the various forms of this disease. Poisoning by decomposed food may also have to be considered. In many cases of poisoning mentioned above we have to deal, as well as in cholera, with poisons whose origin is due to the action of a schizomycete, the only difference being that these latter do not, as the cholera germs, possess the faculty of a general dissemination and of the formation of toxins under varied external conditions. It becomes our duty therefore, in the first instance, to find out whether we may not arrive at a diagnosis by finding the cause. In individual cases, this is done by an examination of the stools and the vomited matter, in other cases it may be accomplished only by a thorough physical investigation. In conjunction with a chemical examination, a bacteriological one is in every possible case to be undertaken.

By the discovery of Koch's vibrios in Asiatic cholera our former difficulties seemed at first to have disappeared altogether, but we were somewhat premature in our optimistic conclusions. That, in spite of the undoubted presence of cholera, an examination for the comma bacillus in the stools should occasionally give negative or doubtful results, is not of so much importance as the fact that the vibrios of Asiatic cholera, in opposition to the early view, may be mistaken for a great number of curved bacteria of like appearance and also of similar growth. Deneke, Miller, and Finkler and Prior have described similar microorganisms, that of Finkler and Prior, however, being the only one of real importance. It has also been shown that the so-called "cholera-red reaction" which in the beginning was looked upon as characteristic, does not possess any specific importance in differentiating the cholera vibrios. The animal experiments at first made use of for the demonstration of the pathogenic properties of the bacillus have not been proved to possess the importance that was at first ascribed to them.

R. Koch, in the year 1893, made the assertion that among all the spirilla which come under consideration in the differential diagnosis of cholera, none had been found up to that time which would produce such a fall in temperature and such fatal symptoms of poisoning as the cholera bacillus. This was shown in certain experiments of Pfeiffer who injected a mixture of 1 c.c. of bouillon and 1.5 mgm. of culture on agar of the suspected microorganism about twenty-four hours old into the abdominal cavity of guinea-pigs weighing about 300–350 gm. It has, however, been shown since then that water bacteria from the various streams of Germany, which may indeed have been contaminated by cholera bacteria, produced the same picture of

severe poisoning. Part of these bacilli, it is true, exhibited the property of phosphorescence, and could thus be differentiated from the vibrios of Asiatic cholera; but even the non-luminous variety, although their differentiation is impossible, are for the present not recognized by Koch as true cholera vibrios.

Pfeiffer has now elaborated another method of differentiation, which he has described as a specific cholera reaction. He made use of the fact that we may, by treating certain animals with true cholera vibrios, obtain in them a degree of immunity, which is shown only against true cholera vibrios, but not against any other bacteria, including those resembling the true cholera vibrios.

A serum is separated from the blood of these immunized animals and injected, mixed with cholera vibrios, into the abdominal cavity of guinea-pigs. The cholera bacilli die within half an hour as a result of this admixture, while other vibrios are totally unaffected by the serum of immunized animals. This observation has been corroborated by Dunbar, and its general value in differentiating other microorganisms has also been demonstrated. Fränkel has been converted to Pfeiffer's view, and Löffler and Flügge also vouch for the reliability of the new method. Gruber has recently recommended as of diagnostic value the phenomenon of agglutination of the cholera vibrios upon admixture with immunizing serum in the test tube. This method must, however, be regarded as yet in the tentative stage as compared with the diagnostic methods at present employed.

The presence of cholera vibrios is now demonstrated by:

1. *Examination under the cover-glass* of a floccule of mucus from the dejecta spread on the glass and properly stained. When pure cultures of comma bacilli are present in characteristic order, a positive diagnosis of cholera can at once be established. Should other bacteria be present besides comma bacilli, the diagnosis is questionable.

2. *Cultures in Peptone* (Koch, Dunbar).—A sterilized aqueous solution of one per cent. peptone and one per cent. common salt which has been rendered strongly alkaline, and diluted with one or more drops from a platinum rod of the liquid to be examined, is placed in the incubator at 37° C. The cholera bacteria, as Schottelius was the first to point out, have a tendency, on account of their great desire for oxygen, to come to the surface of the culture fluid and rapidly increase here. A pure culture of comma bacilli, occasionally contaminated with the bacterium coli, is frequently found on the surface of the solution of peptone six to twelve hours after the setting of the culture. In doubtful cases this method may be supplemented by the following.

3. *Cultures on Gelatin Plates.*—The proof is furnished by mixing

a floccule of mucus with a ten-per-cent. solution of gelatin in an incubator at 22° C. The colonies of comma bacilli will present a characteristic appearance after forty-eight hours at the latest; microscopic preparations of these colonies will give a pure culture. In place of Koch's culture medium Deyke has recently proposed another, which contains as an essential and specific constituent alkali-albumin. This culture medium may be designated as an elective one for cholera bacilli, but it does not permit of any differentiation between them and Dunbar's vibrios.

4. *Cultures on Agar Plates.*—These will often yield a surface inoculation after having been placed from eight to ten hours in the incubator at a temperature of 37° C.

5. *The Cholera Red Reaction* (*nitroso-indol reaction*).—Pure cultures of comma bacilli yield a red color upon the addition of sulphuric acid (in the absence of nitrous acid).

6. *The Agglutination Test.*—Three milligrams of an agar culture, fifteen hours old, are carefully mixed with 0.5 c.c. of bouillon. After this, 20 mgm. of serum from a guinea-pig highly immunized against the cholera vibrios are added to 0.5 c.c. of sterilized bouillon and the two fluids are mixed. This mixture is at first uniformly turbid. If after a few minutes this turbidity becomes flocculent, and a deposit is formed after one hour, the reaction strongly points to the presence of cholera vibrios. The same change may be observed in the hanging drop.

7. *Pfeiffer's Animal Experiment with Immunized Serum.*—Blood serum taken from guinea-pigs or goats, which have been rendered immune in the highest degree by treatment for many months with cholera bacilli, is greatly diluted with simple culture bouillon (in the proportion of 1 : 100). This mixture represents the reagent. A loop taking up about 2 mgm. of an agar culture, twenty hours old, of the kind of vibrios to be examined is now mixed evenly with 1 c.c. of the mixture of bouillon serum just mentioned and the culture thus obtained is injected into the abdominal cavity of young guinea-pigs weighing about 200 gm. Every five minutes a few drops of the contents of the abdominal cavity are withdrawn by means of capillary glass tubes passed through the abdominal wall, and are examined in the hanging-drop and in stained cover-glass preparations. The true bacteria of cholera are in this experiment changed by the action of the cholera antitoxins into peculiar, pale, rounded bodies, which are wholly soluble in the fluid of the abdominal cavity without leaving any residue. This solution, occurring with the accuracy of a chemical reaction, is accomplished in the space of twenty minutes, providing the cholera serum is active.

If we should still find after this time numerous unchanged and moving vibrios in the specimens from the peritoneal contents, these are positively not cholera bacilli, but a foreign species of vibrio (negative result of the reaction). If, on the other hand, we should find all of the comma bacilli destroyed, we must yet decide between two possibilities: we are either dealing with a true culture of cholera, which has been specifically influenced by the bactericidal effect of the antitoxins of cholera (positive result of the reaction), or we are dealing with one of those saprophytic cultures of vibrios which are so deficient in all pathogenic action that they also succumb quickly to the antibacterial influences already present in the normal body of the guinea-pigs, without the necessity of any specific action of the serum. A control animal, which is injected with one loop of the culture in question, mixed with 1 c.c. of bouillon and 1 mgm. of normal serum, will give us the answer. If the vibrios are still found alive and moving in this control guinea-pig at a period when the bacteria are fully dissolved in the cholera-serum animal, the fact that this is the true cholera variety of comma bacilli may be considered as proven.

Prognosis.

The prognosis, as may be concluded from all that has been stated in the foregoing, is dependent on the gravity of the symptoms. According to this the mere infection of cholera without any marked symptoms of disease will, with proper care, give no occasion for anxiety, and in the same manner in a case of simple choleraic diarrhœa, occurring in a person of good constitution, if the patient receives proper treatment we may look forward to a favorable issue. We must nevertheless always be prepared, in children, invalids, and those who are weakened by overwork or by the abuse of alcoholic beverages, for the probable aggravation of the disease. As some epidemics of cholera are ushered in with prodromal diarrhœas, which lead after a number of days to cholera gravis, it behooves us also to be non-committal in our prognosis at such times. Cholerine, as a rule, also takes a favorable course, as we have learned from the experiences of former epidemics (Lebert) and also of that of Hamburg. But this affection may lead to death in debilitated patients.

The prognosis of the *grave* cases of cholera is naturally a very doubtful one. As a general rule, persons between the ages of five and twenty-five years present the best prospects of cure. So many and various factors are, however, to be considered here that it is hardly possible to foretell the result, in any individual case, during the attack itself. A patient may be left in a seemingly moribund

condition, and an hour later may have nearly perfectly recovered; and another, who seemed less sick, may now be in the severest algid stage. The resisting-power of the body against the specific poison of cholera is the main factor here. Occasionally also a person may recover, the state of whose health or whose previous habits may have led us to expect an unfavorable issue. Furthermore, the character of the epidemic must be taken in consideration in the prognosis; in large epidemics also the time of the attack, whether it occurs during the ascending or during the descending curve of the epidemic.

The individual symptoms are of smaller moment in this regard. That a patient is suffering with copious evacuations or vomiting is not positively an unfavorable sign. More frequently those cases in which the picture of cholera gravis very rapidly develops in the absence of marked diarrhœa run an unfavorable course. That in cases presenting violent and especially involuntary dejections, rapid exhaustion, great anxiety, deep cyanosis, moist and cold skin, and an absent or extremely weak pulse, the prognosis is unfavorable, follows naturally from what has been previously said. If the bodily temperature now becomes lowered, and the second cardiac sound inaudible, a lethal ending is to be expected almost with certainty.

So also the occurrence of bloody, fetid stools, which probably always point to the presence of ulcerations and necrotic processes in the intestine, and hæmatemesis caused by hemorrhagic infarctions of the stomach lead to the worst prognosis. Abortion also, occurring during an attack of cholera in the pregnant woman, seems to diminish the prospect of recovery. The suppression of urine cannot be looked upon *eo ipso* as an unfavorable sign. A normal excretion of urine in a typical attack of cholera is very rare and when present may be considered a favorable sign.

The complication of an attack of cholera with pneumonia seems to warrant an unfavorable prognosis, and so also does an existing case of typhoid fever complicated by cholera. In the latter combination a favorable issue has, however, been observed. After the attack of cholera has passed, the patient is by no means yet safe, and at this time the prognosis is frequently still more difficult as the possible occurrence of coma places life in great danger. It is important, in this relation, to observe whether a febrile reaction follows the attack, as this presents an essentially more favorable indication of recovery than a prolonged or suddenly occurring subnormal temperature. A slight fever is frequently accompanied by a certain somnolence, which as a rule disappears with the eruption of an exanthem and rapidly leads to recovery. On the other hand, grave coma is frequently developed with the occurrence of a subnormal temperature. With

this the pulse may be full and the face congested. The congestion, however, soon disappears, the color again becomes of a pale gray tint, and death takes place in stupor. From older epidemics we have the record that in these cases the continuation of diarrhœa and involuntary evacuations has been observed, and our own observations have demonstrated that these evacuations still regularly contain comma bacilli. On the other hand, we would point out that when the cases take a favorable course, the vibrios rapidly disappear from the stools. We undoubtedly also meet with individual cases of slight choleraic diarrhœa in which the bacilli may still be present for a long time. But these cases give room for the fear, as has also been stated, that some irregularity in the behavior of the patient may bring on a grave attack. In cases of true cholerine and of cholera gravis accompanied by severe symptoms, but going on to a favorable issue, the stools, as a rule, do not contain any cholera bacilli after the course of a few days, while the bacilli always remained present in the continued diarrhœa in cases of grave coma.

Therefore, the results of the bacteriological investigation are very essential in the prognosis of cholera. If, after the attack has passed, comma bacilli are still found in large numbers in the dejecta the appearance of a grave coma may be predicted with great certainty. At all events, it would be desirable that this experience gathered during the epidemic in Hamburg should be controlled by still further investigation.

Prophylaxis.

History.

The vast desolation which was caused by cholera, in six great pestilential invasions, in Asia, Europe, Africa, and America was the reason why general and individual protective measures assumed great importance in cholera earlier than in most of the other infectious diseases. The different views as to the course of the infection, however, soon led to altogether opposite hygienic measures. The fact that some small localities coming little in contact with the outer world through commerce had remained free from cholera was the occasion of whole countries being barricaded by military cordons and of the enforcement of the strictest quarantine. Nevertheless, these measures were frequently insufficient to keep the plague from invading the threatened territory. It thus came to pass that these rigorous measures of quarantine were rejected as useless by most representatives of science and by the governments. Von Pettenkofer, who has done work of the greatest value in the epidemiology of cholera, declared on

the basis of careful investigation that cholera was not a contagious disease, that its importation into a locality could in no way be prevented, and that still other factors than the presence of cases of cholera were necessary for the appearance of an epidemic. These auxiliaries of cholera, which consist especially in a defective public and private hygiene, were to be overcome, and only general sanitation had the power effectively to prevent the dissemination of the plague. In opposition to these views, R. Koch, Gaffky, Flügge, and others maintain the possibility of a direct transference of cholera from one person to another, and hold that, aside from general hygienic measures, special precautions are necessary in the prevention of the spread of the disease. These views of Koch and his pupils have led to the adoption of careful prophylactic measures on the part of the state. Notwithstanding the fact that the disease raged in part with its old-time violence in Russia in the years 1893, 1894, and 1895, and that various importations resulted, especially through maritime intercourse, Germany remained free from any actual epidemic. These happy results furnish sufficient ground for us to continue in the way we have begun. In the same manner prophylactic measures were taken by the United States as regards maritime intercourse with Europe, and that country also remained free from an epidemic invasion.

State Prophylaxis.

The most efficient state prophylaxis would consist in a perfect prevention of cholera invasion. These measures, however, can be carried out only in countries which have intercourse with infected regions through but a few widely separated ports. Even under these conditions, however, rules for barricading and quarantine have failed, in a number of instances, to prevent the invasion of cholera. An importation of cholera cases is hardly to be prevented on the mainland, as is already clear from the fact that seemingly perfectly healthy persons may be the carriers of cholera, and also that the water of streams may carry the germs which have been deposited in it to localities which had peviously been free from the disease, without regard to any frontier barricades. For this reason, a strict quarantine against infected districts, which so readily tends to inflict great injury on national prosperity, must be rejected as useless and harmful. Nevertheless, the sanitary police should not be altogether without authority in watching over commerce. If travellers arriving from districts infected by cholera, especially when there was a suspicion that they themselves might be suffering from cholera, were isolated for a sufficient period or until the dejections were

found to contain no germs, a check would certainly be put on the dissemination of the cholera poison. We should also have to consider those as liable to cholera in this case who had come in contact with cholera patients, but were themselves healthy. How long these persons should be kept in quarantine may be doubtful. The German Empire requires a supervision of five days. The United States insist that passengers who have been together with cholera patients on board a vessel which has arrived in port be quarantined at least five days. If a vessel having cholera patients on board arrives, quarantine is frequently greatly prolonged. That an attack of cholera may occur even after a surveillance of five days cannot be doubted, although such cases are certainly quite infrequent. A case of cholera appearing after this time, however, would not remain concealed if the reporting of such cases should be strictly enforced, and if lodging-houses and hotels, which are particularly adapted to the spread of the disease, should be subjected to special sanitary supervision.

The same care which is accorded the cholera patient and the cholera suspect should, however, also be given to all ships and their cargoes arriving from infected localities. If, according to Nocht's suggestion, vessels should always be kept under sanitary surveillance while in port, this surveillance will be doubly necessary for vessels coming from infected localities. An examination must be made especially of the water which is in the ship's tanks. Dry rags, clothing, and soiled linen are probably less responsible for the spread of the disease than was formerly supposed. Perfectly dry goods, according to all past experience, should also be considered harmless. On the other hand, fruit, potatoes, vegetables, milk, butter, and cheese must all be looked upon as culture media for comma bacilli, although in most of these the vitality of microorganisms is restricted. Beer, wine, alcoholic beverages, natural mineral waters, may on the other hand be considered as perfectly safe, and artificial mineral waters containing large quantities of carbonic acid gas allow the comma bacilli only a very restricted vitality. According to all experience, especially that of recent epidemics, water must be considered as peculiarly dangerous. Water which has been brought, either as drinking-water or as ballast, on ships from an infected port should be carefully disinfected. By reason of the ability of the comma bacilli to retain their vitality for a long time in water, even at a low temperature (Uffelmann and others), and to increase when the temperature is again raised, and in the presence of a certain richness of the water in organic ingredients, particular attention should be accorded this method of the spread of cholera. That the dejecta

coming from suspected vessels and the underclothing of cholera suspects should be kept out of the water of the river or harbor it is hardly necessary to mention.

The next duty of state prophylaxis consists in the institution of measures to prevent the spread of comma bacilli in case of the discovery of imported or recent cases of cholera. It is therefore of the greatest importance that each individual case in which there is the slightest suspicion of cholera should be most minutely examined. The examination is best carried out by a number of persons. Every physician who realizes the results of the diagnosis of a cholera case at a period when no cases of the disease have yet appeared in the locality will most certainly consult with the health officers as soon as possible, and the state has a right to demand this, in view of the consequences of such a diagnosis. To strictly enforce the reporting of cases of cholera and of cholera suspects is therefore the first measure of state prophylaxis. After a case is once recognized as cholera, it will be so much the easier to prevent the spread of the plague the sooner the diagnosis is made. For this purpose cholera patients should be isolated in a special hospital or a special ward, and so also should all those who are carriers of comma bacilli without presenting essential symptoms of disease. We must take into consideration in the arrangements to be made that the spread of the disease is caused by the dejecta and perhaps also by the vomited matter. Accordingly the dejections, as well as all vessels used by the patient, the bedding, and the clothing should be carefully disinfected before he is allowed to mingle with healthy persons. Disinfection of the vessels is best brought about by boiling them well; the dejecta are best mixed with a solution of lysol, carbolic acid, or kresol, in the proportion of about five per cent. This mixture is allowed to stand about one hour. All linen used should be placed in a three to five per cent. solution of lysol, and remain in it from one to two hours. Bedding and clothing are best disinfected by steam. In the absence of a steam disinfecting plant, they may be washed in a five-per-cent. solution of lysol and then dried in a very hot place for three or four days. The apartment inhabited by a patient should also be disinfected before being used for other purposes.

For this purpose all movable articles are to be taken out of it, and disinfected either by steam or by washing well with a three to five per cent. solution of lysol. The empty room is then to be scrubbed, as well as may be, with a five-per-cent. solution of lysol, the walls rubbed down with bread and where possible freshly whitewashed or painted. After again cleansing the floor with a five-per-cent. solution of lysol and drying, the room should be allowed to

remain empty for at least three days, being during this time heated. Instead of lysol, the other disinfectants mentioned above may be used for this purpose. Articles of little value which have come in contact with the patient are best burned. We must, however, bear in mind that the articles to be burned should not be moved to other places, carrying the germs of the disease with them. That the nurses of cholera patients should not eat or drink in the sick-room, that they should remove their infected clothing when visiting or going to meals, should carefully disinfect their hands and face, and then change their clothes is so evident that it need hardly be insisted upon.

If cholera has broken out in a house in which is a shop for the sale of food, the business must at once be closed. If these measures are to yield good results, moreover, they must be carried out at once on the appearance of a suspicious case.

The bodies of patients who have died from cholera should be allowed to remain in the house where death occurred only if all these measures against the spread of the disease can be taken. Washing the dead is best dispensed with, or should be done with a lysol or kresol solution. The bottom of the coffin should be covered with peat or sawdust, and the body should be wrapped up in a cloth saturated with a solution of corrosive sublimate or carbolic acid. In this condition it is to be taken to the dead-room or the cemetery. Exposing the body to view is better dispensed with. The undertaker must carefully disinfect himself in the same manner as ordered for the nursing staff.

In every case of cholera search should be made for the source of the disease, and this must be rendered innocuous. Frequently we shall then come across other cases which have been overlooked, and which may lead to a spread of the infection, or have already done so. For this reason a surveillance of all the dwelling-houses in which cholera cases have occurred is a pressing necessity. Frequently these houses are in need of thorough disinfection and should be examined as to their sanitary condition as regards water-closets and plumbing, the position of hydrants, and the water-supply. In the mean time the inhabitants must be taken to a temporary quarantine station. The public water-closets also, in view of their probable infection by cholera dejections, stand in need of special watching and regular disinfection.

A third very important duty connected with state prophylaxis is the surveillance of dealers in food products. Spoiled or suspicious food must be destroyed. Dealers in milk should be under sanitary control, and especially should means be taken to prevent dilution of the milk with water. Ice should be allowed for sale only if it is ab-

solutely free from suspicion, coming from uncontaminated streams or lakes or made artificially from distilled or pure spring water.

Especial care must be devoted to the question of drinking-water. The drinking of river and harbor water, which is always to be condemned, should be especially warned against in times of cholera. In cities where the dwelling-houses are supplied with water that has not been filtered, the boiling of all water used for drinking or other purposes should be insisted on. Water which has been filtered may still contain cholera germs, although perhaps in smaller number, and it is therefore well when cases of cholera appear to recommend the boiling of the water at once. That it is the duty of the government to supply the people not only in times of cholera, but also at other times, with a perfectly pure drinking-water, goes without saying. The filtration through sand, now in use, can by no means be considered an absolute solution of this certainly very difficult task.

Parallel with the question of a supply of pure water is that of the disposal of fecal matter. The example of Hamburg has, however, shown that a good system of sewerage alone is not sufficient. It is also the duty of the government to prevent the infection of rivers by cholera germs. In this relation a careful control of ships and their inhabitants is above all necessary. Whether it be possible to compel sailors not to throw discharges into the river strikes me as problematical. Wherever, however, seamen, raftsmen, and fishermen are required by law to carry pure water not only for drinking but also for washing dishes, it is certain that infection is frequently prevented. It is to be recommended besides that all vessels should be under constant supervision. This may be accomplished at the ports of embarkation and arrival, and in river boats also at certain intermediate points. A control of this kind of necessity would interfere with commerce only where grave danger is threatened. All vessels, however, must at all times be subject to certain sanitary laws.

The methods of disinfection of cesspools and of the mouths of sewers discharging into rivers should be very different from those at present employed. We should not forget that the water of a river is a better culture medium for microorganisms in porportion as it is richer in organic constituents. That in times of cholera the disease may be spread far and wide through the aggregation of many people at fairs must be considered. The Mohammedan pilgrimages are especially notorious in this relation. The surveillance of vessels on which pilgrims travel has of late been undertaken, but the large numbers of pilgrims and their stubborn opposition to such measures present a great obstacle, and consequently it has seldom been possible to prevent a spread of the disease from Mecca to Egypt. If the surveillance

would, however, be carried over a larger territory and with greater strictness, the result would in all probability be much better. For the same reasons, it is also unwise to have large army manœuvres, during times of epidemic, and in localities where cholera is raging.

The public administration in times of cholera, however, has still greater opportunity, aside from these duties, to show its vigor and its ability. The insuring of medical attendance and nursing, visits from house to house by committees or individual members, the erection and enlargement of kitchens for the people, etc., would relieve much suffering occurring in the course of the epidemic, while it would, on the other hand, conduce to the limitation of the epidemic by the discovery of infected material.

The giving of full instructions to the public concerning the nature of cholera and its dissemination by the excreta and by filth is, however, also to be desired. At the same time we should recommend the carrying out of individual measures of prophylaxis.

Personal Prophylaxis.

Personal measures of precaution consist, first, in the care that no food or drinks contaminated with comma bacilli should enter the digestive tract; secondly, in leading a regular life, free from excesses in eating and drinking, so that the body may retain the faculty to eliminate or destroy any comma bacilli which may by chance have gained access, before they can cause a severe disease. As regards the first it is necessary to wash the hands before each meal, to take food and drink only after it has been cooked or boiled, and in a perfectly good condition, and also to keep the dishes used at meals free from infection by washing them in pure or in boiled water. In particularly dangerous places, a disinfection of porcelain or glass wares may be obtained by boiling. Bread and other cold foods which are not to be trusted to be uncontaminated may be freed from viable comma bacilli, which might have adhered to them, by scorching. Bread may be thoroughly disinfected by heating it for one hour in an oven at 70° to 80° C. (158° to 176° F.). Although we should limit our consumption of food as nearly as possible to cooked substances (although wine, good beer, and mineral waters are not excluded), it is, however, well to adhere to our ordinary mode of life as nearly as we may. An essential change in the diet is not good, for the simple reason that a disturbance of the digestive functions might thereby easily be induced which would greatly facilitate the arrest and growth of the comma bacilli. That excessive regulation of the diet involving radical change in the mode of life is especially dangerous should be empha-

sized repeatedly. Acute and chronic alcoholism must be named above all others as the cause of a particular disposition towards grave choleraic attacks. Persons who are debilitated from other causes must also be exceedingly careful in their measures of prophylaxis. A warning does not seem out of place here to avoid strange and especially suspected water-closets, to refrain from visiting localities and houses which harbor cholera patients or cholera suspects, although we have no positive proof that cholera has ever been conveyed in this manner. The closing of the schools would hardly be necessary in cities where good sanitary laws are in force. It would, however, be well to organize a system of sanitary inspection in all places where a great number of people daily congregate, as in schools and factories, and to inquire daily whether any case of diarrhœa had occurred. Any ailing person would then be given at once into the hands of a physician. Whether we shall be able hereafter to prevent extensive cholera epidemics by these prophylactic measures coupled with progressive sanitation of cities must be left to the future to determine. For the present, it is without doubt too early to cherish a sure hope, for the mode of infection is by no means always so open and clear to us, as is taken for granted by some.

The Spanish physician Ferran was the first who tried in the epidemic of 1885 to afford individual protection by subcutaneous injections of cultures of virulent cholera bacilli and of the blood of convalescents. The experiments of Gamaleïa, Zäslein, Löwenthal, Brieger, Kitasato, Wassermann, and others demonstrated that the blood of animals that had been treated in this manner really acquired immunizing properties. This immunity, as already previously mentioned, consists, according to the researches of Pfeiffer, in the formation of specific antitoxins in the blood, which paralyze the cholera vibrios or destroy them. Haffkine also has made many experiments in this direction and has devised a method for attaining individual prophylaxis by the subcutaneous injection of cholera cultures.

During the years of 1893 to 1895, about 50,000 persons have been treated after Haffkine's method, and the results of this treatment are not unfavorable. At all events, the mortality of those inoculated was very small. Thus, 202 persons were inoculated in one prison, 207 were not treated. Among those not inoculated 9.9 per cent. had cholera and 4.95 per cent. died; among the inoculated 3.39 per cent. suffered an attack of the disease and 2.41 per cent. died. Kitasato also prepared an antitoxin and tried it on cholera patients in Japan, but with what success we are not yet able to determine with any positiveness. But in any discussion of this method it is in place to ask whether the antitoxins of the blood are still able to exert their influ-

ence on the bacilli which have entered the intestine, when the symptoms are already fully developed; whether, in other words, we have here a curative as well as a prophylactic method. The results of further experiments must determine whether the method is efficacious. If so, it would then be of great service in the endemic home of cholera. Haffkine's experiments have certainly been supported by Kolle's findings of protective substances in the blood of persons treated in this manner, so that the prophylaxis of cholera has been essentially enriched, as regards the countries where this disease is endemic. For other countries this would not come into consideration in the absence of an epidemic.

Treatment.

For a long time the therapeutic speculations of physicians and laymen played an important part in the treatment of cholera. The more obscure the cause of cholera was the more the called and the uncalled felt justified in making themselves heard. Above all was it the hunt after specific remedies which occupied the chief place. Together with this, the greed of gain was also an impelling factor, and this has found at the present time a new field of activity in the vaunting of a host of chemical preparations. Nevertheless from the earliest epidemics there have been some who, ignoring the clamor of the time for specific medication, argued in favor of a general therapy. In this connection I cannot refrain from mentioning a communication made by Schaefer in the year 1831, which was made public by Rust. I shall find occasion in another place to give some special extracts from Schaefer's paper.

The possibility of discovering a specific cure for cholera can certainly not be denied. We may look for advance in this direction, above all, to modern bacteriology. Much preliminary work will, however, have to be done in this study before our hopes can be realized. At all events, the experiments of Kolle and others, as well as the researches of Haffkine, permit us to hope that the treatment of cholera will receive an essential advance from the studies of Ehrlich and Behring.

Cholera Infection without Marked Symptoms.

The treatment of cholera infection, in the absence of any marked symptoms of disease, will only very rarely come in the physician's way; for, as a rule, this condition is discovered only by accident. Numerous examples nevertheless testify to the not altogether infre-

quent occurrence of this form, and from this point of view we should regard and enforce all those general hygienic measures which have already been discussed under the heading of individual prophylaxis.

Choleraic Diarrhœa.

Every person suffering from "choleraic diarrhœa" or every person suspected of it, should rest in bed and be kept warm. Often the affection goes on to recovery under this management before a bacteriological diagnosis has been made. This cure is substantiated by the fact that the stools become less frequent and again take on a feculent character. Comma bacilli may perhaps be found in the first or the first few stools, but these soon succumb to the action of the normal decomposition processes in the intestinal contents. In this connection it may be of interest to know that the comma bacilli cannot develop when there is even the smallest amount of indol and skatol present in the culture fluid (Rumpel). Thus a restitutio ad integrum takes place without any medicinal interference.

How frequently a spontaneous cure may occur, and how frequently the comma bacilli pass through the intestinal canal without giving rise to essential symptoms of disease it is of course impossible to say, as cases of this kind are only exceptionally admitted to the hospitals or examined bacteriologically. In the mean time we are furnished with a few interesting points at least by the searching investigations made at Hamburg in the summer and autumn of 1893. Among 150 cases, in which a diagnosis of Asiatic cholera was made as a result of the presence of comma bacilli, only 80 displayed the typical symptom complex; in 36 cases there was diarrhœa accompanied by one or more attacks of vomiting, in 24 cases there was present only a diarrhœa of varying intensity. Some of these patients recovered, without any medicine, while pursuing their usual occupations. In 1 case comma bacilli were present in a perfectly healthy man, and in 9 cases as a chance complication, unaccompanied by cholera symptoms, in other diseases. These findings certainly prove that comma bacilli may pass through the gastrointestinal canal in a great number of people without causing any severe disturbances. It is, however, not always that the cure of choleraic diarrhœa is accomplished in this simple manner.

Physicians have from the first sought to check the most essential symptom of the disease (the diarrhœa) by opium and thus accomplish a cure. Opium with or without a combination of astringents or aromatics has for years taken first rank, especially in the mother country of cholera, in the treatment of the disease, particularly in the

early stages. The "astringent pills" furnished to the people by the English government in times of epidemic recrudescence, contain opium, asafœtida, black pepper, and camphor. Schaefer in 1831 recommended an infusion of peppermint, a glass of which was to be taken warm, with the addition of two drops of Sydenham's laudanum, every fifteen minutes. If we take into account the possibility of a spontaneous cure by a reversion to the normal intestinal functions, the favorable influence of opium conjoined with remedies which excite the functional activity of the intestine may in some cases be explained. Observations have, however, also been made which do not present the treatment by opium in an altogether rational light. It was possible, it is true, to check the diarrhœa for a number of hours, but it recurred when the extreme effect of the opium passed off, and led to greater disturbances or necessitated, on account of the debilitated condition now occurring, other therapeutic interference. In isolated cases, however, the picture of a grave attack of cholera, either with or without the appearance of a profuse diarrhœa, followed this opium treatment. This occurrence renders it plausible that the quieting of the intestine thus produced in the first instance may be the cause of an increase of the comma bacilli or of an intoxication brought about by the absorption of the cholera poison. The latter might readily occur, especially in those cases in which the epithelium of the small intestine is necrosed. From this point of view, we are not altogether justified in administering opium with the object of quieting the intestine solely on the ground of the existing diarrhœa, without any further consideration. Opium, it is true, possesses other properties than this. Together with its influence on the general nervous system we must also ascribe to it a direct or indirect influence on the spasmodic conditions of the smooth muscular fibres. Irritable conditions of the latter are present among the symptoms of cholera in the circulatory system, and in the intestine itself. Partial spasm of the smooth muscular fibres of the intestine may here, as well as in other forms of intoxication, be the cause of a partial retention of the intestinal contents, while the profuse diarrhœal discharges lead one to believe that the intestine has been almost entirely emptied. A lowering of this excitability of the intestine by opium may exert a favorable influence in this way, but it should not be so strong as to produce absolute constipation. The patient usually comes to the physician on account of the diarrhœa, and treatment for this is demanded long before a diagnosis of choleraic diarrhœa can be made. In cases of this kind, there is certainly no objection to the administration of small doses of opium, so long as the presence of large fecal accumulations is not demonstrated by intestinal distention. As only small doses are indicated,

the following formula may perhaps be useful in the case of an adult, beside the remedy mentioned above by Schaefer:

℞ Tincture of opium..... 5.0 (ɱ lxxv.)
Compound tincture of cinchona..... 50.0 (ʒ iss.)
M. Sig. : A teaspoonful to be taken as ordered.

Or,

℞ Tincture of valerian..... 20.0 (ʒ iv.)
Compound elixir of orange,
Aromatic tincture..... āā 15.0 (ʒ iij.)
Tincture of opium..... 5.0 (ʒ i.)
M. Sig. : Twenty to twenty-five drops to be taken every two or three hours.

The opium may also be combined with mild laxatives:

℞ Opium..... 0.02 (gr. ⅓)
Calomel..... 0.05–0.3 (gr. ¾–5)
White sugar..... 0.05 (gr. ¾)
M. Sig. : One such powder every three hours.

In the epidemic at Hamburg, in 1892, opium was, however, also exhibited in a different manner on recommendation of an English physician, Dr. Wall, who had employed it in numerous epidemics in Calcutta. Reiche injected about fifteen drops of the fluid extract of opium subcutaneously, not so much in recent choleraic diarrhœa, as in cases which threatened to pass into the cyanotic stage. In a number of cases a favorable influence on the circulation, a disappearance of the cyanotic hue, and an improvement in the pulse were plainly visible.

Turning from the opium treatment, the thought arises, as an outcome of modern scientific research, that the introduction of antiseptic remedies into the gastrointestinal canal might check the growth of the comma bacilli and prevent the development of the symptom complex altogether. All the measures which rest solely on this indication cannot, however, be signalized as successful. Attempts in this direction were probably made for the first time by von Leyden in the Königsberg epidemic, without any essential good results, however. In the same category we must also place the use of chlorine water, which was recommended as a specific by Dyes. The experiments which we made at the beginning of the Hamburg epidemic with chlorine water gave such discouraging results that they were soon abandoned. No more favorable results were reported by the physicians of the cholera hospitals in Hamburg following the use of bismuth, tannic acid, salicylic acid, pyoktanin, creolin, creosote, and preparations of cresol. The same may be said of salol. After Hüppe and Löwenthal had recommended its employment in cholera

on theoretical grounds, and Löwenthal had even praised it as a specific, it is not surprising that it was administered in large quantities both by the stomach and by subcutaneous injection in the form of salol ether during the cholera epidemic at Hamburg. A favorable influence on the disease was not, however, observed.

Hüppe then recommended tribromphenol-bismuth as a remedy in cholera, based on his experience in the New General Hospital at Hamburg. The statistics gathered by his assistants Bargum and Boltz show a mortality of the cases treated by him after this method of 53.57 per cent., while during the same period the average mortality in all the cholera hospitals was less than fifty per cent.; it should be added, however, that many of the very grave cases were placed under Hüppe's care. As, however, the worst cases of cholera were at that time generally taken to other hospitals (and not to the New General Hospital, which was situated at a distance from the centre of the infected district), the results of Hüppe's treatment would hardly encourage one to continue with the same method, or even to regard intestinal antisepsis, which by the way has yielded only very few good results, as the rational mode of treatment of cholera. This failure of an apparently rational measure is somewhat surprising. The explanation is, however, probably to be found in the fact that with the destruction of the comma bacilli in the intestinal canal, the absorption of the toxins from here into the body is, owing to the desquamation of the intestinal epithelium, not prevented. It is also probable that the comma bacilli which invade the wall of the intestine in great numbers are affected to only a limited degree by the remedies introduced into the intestine.

The employment of muriatic and lactic acids (the latter recommended by Dujardin-Beaumetz) has not in our experience given any very good results. In a few cases the gastric and intestinal contents as far as Bauhin's valve were, it is true, made distinctly acid by the ingestion of large quantities of acids; it was nevertheless possible to cultivate comma bacilli in these acid gastric and intestinal contents, obtained at the autopsy. Although the fatal issue was not prevented in some cases in spite of a copious supply of acid, nevertheless I am very partial to the administration of a solution of citric acid as a drink, together with other remedies, and I believe that I can at least say that no injury will result from this practice.

After this unfavorable experience in modern gastric and intestinal antisepsis, we had recourse again to an old treatment, based upon the belief that the most radical removal possible of the comma bacilli from the intestinal canal is a primary indication. As Lebert informs us, Jules Guérin as early as 1849 treated every case of cholerine with

castor oil, and after that it was also used in England very extensively. One to two tablespoonfuls, according to the age of the patient, will in most cases be sufficient.

Together with castor oil, calomel has also been given for the same purpose. In the employment of calomel we have to bear in mind that probably an antibacterial effect is produced by the formation of a small amount of corrosive sublimate. The exhibition of calomel in the treatment of cholera is not altogether new. Reports of its employment by English physicians date from the end of the thirties. In 1840 Amelung discussed the question whether calomel might not be of service in cholera if given in small doses, and towards the close of that same decade the drug was again warmly recommended, especially by English physicians, by Stedman, Allan, Allen, and Roger. Felix Niemeyer made extensive use of it in the Magdeburg epidemic, and Leyden in the Königsberg epidemic; von Ziemssen also warmly recommends it. The doses employed by the individual authors varied. At times large single doses (0.3 to 0.5 gm. = gr. v. to viiss.) were recommended, administered three times and followed by smaller doses; at other times very small doses (0.03 to 0.05 gm. = gr. ss. to i.) were recommended. In the Hamburg epidemic both ways of administering calomel were tried. As, however, typical intestinal and renal symptoms of mercurial poisoning were observed in two cases treated with large doses of calomel, I would recommend the employment of the smaller doses (0.03 to 0.05 gm.—gr. ss. to i.) every two hours. This treatment should be continued one or two days. As a rule, only a slight increase in the number of stools is observed. At first these are usually not changed in color, at all events there has seldom been observed any green discoloration, but frequently the discharges assume a yellow or brown color in the course of the next few days. In this manner an adult receives from about 0.6 gm. (gr. x.) to at the most 1 gm. (gr. xv.) of calomel in two or three days. These doses, which should be somewhat less in children, are probably sufficient for the purpose intended.

Besides the employment of calomel, we occasionally tried the administration of the sulphates in combination with organic acids. We were in hopes that the increased peristalsis would also lead to a rapid transportation of acid into the intestine and thus lead to a still further diminution in the number of comma bacilli. The combination of citric acid with Epsom salts was taken with great reluctance, and furthermore we also failed to get the expected increase of the intestinal discharges, so that this method of treatment was very soon abandoned again.

This treatment of choleraic diarrhœa with purgatives, just outlined,

can naturally be carried out only for one or two days. Frequently diminution in the number of the discharges, the latter also assuming a yellowish tint, occurs spontaneously. If this does not happen, there is danger that the dilatation of the abdominal vessels will be increased by the continued peristalsis of the irritated intestine, thus occasioning a diminished blood supply in the rest of the circulatory system, and a lessening of the exchange of gases in the lungs. The pulse of the patient will be the guide for this change in treatment. Should it be accelerated and small, we must not delay in quieting peristalsis, and making some impression on the circulation. It is greatly to be recommended to begin this with a subcutaneous injection, but we may also make use of the internal administration of opium as above mentioned.

In conjunction with this treatment, we must now consider the tannic acid enteroclysis of Cantani. Cantani introduced this method in the treatment of intestinal affections in 1870, and applied it especially in cholera, because according to his experience the Neapolitan tanners suffered very little or not at all from cholera during the epidemics, while the tanners of glove leather, who use no tannic acid, were very much affected by it. He attributed the action of enteroclysis to the fact that the liquid frequently passes above Bauhin's valve, and thus enters into the small intestine, where it is believed to develop a disinfecting and astringent action, the experiments of Manfredi and de Simone having shown that tannic acid exerts a destructive action upon comma bacilli. According to Cantani's directions, 1 to 2 litres (quarts) of a one-per-cent. solution of tannic acid at a temperature of 40° C. (104° F.) is passed through an irrigator into the rectum several times a day. I would add from personal experience that it is well to make the irrigation under slight pressure and as slowly as possible; we then frequently succeed in forcing the ileocæcal valve, and directly flushing out the small intestine. The number of cases in which this succeeds does not, however, seem to be large. Quite frequently the fluid is discharged a short time after it has been passed into the bowel, and we are unable, despite all exertions, to introduce a notable quantity of fluid into the intestine. Nevertheless, the favorable action of the irrigation cannot be denied. In many cases it is followed by a quieting of the intestine, either from the action of the tannic acid or from the heat applied, and in some cases a distinct improvement of the heart's action can be demonstrated, so that this method may be recommended warmly as practical and easy of performance. The experiments undertaken by us to replace tannic acid by other medicinal substances, such as creolin, were not more successful than Lustig's experiments in the Trieste

cholera epidemic of 1886. We also substituted soap in place of tannic acid, on the recommendation of an American physician, Dr. Lee, but cannot say that this possesses any therapeutic advantage over tannic acid. More recently von Genersich has recommended an irrigation of the digestive tract from the rectum upwards, called by him diaclysmus, using a much larger quantity of fluid (5 to 15 litres of a 1 to 2 per-mille solution of tannic acid). This fluid was heated to 38° or 40° C. (104° F.) and used at a pressure of 80 to 100 c.c., the anus being strongly compressed around the rectal tube. The irrigation is occasionally interrupted on account of the discomfort to the patient, but may usually be resumed after a short while. After some time copious vomiting of the irrigating fluid takes place. In this manner as many as 15 litres may be allowed to pass through. When the irrigator is now removed a large quantity of the fluid of course flows away, but 1 to 2 litres will remain behind. The results obtained by von Genersich were quite remarkable. We would decidedly recommend the use of this modification and extension of Cantani's enteroclysis in any future epidemic. Whether it would be feasible in many cases to carry out the irrigation under so high a pressure must be left for future decision.

Cantani's recommendation to begin the irrigation in an early stage, and on recurrence of the diarrhœa to continue with it for several days, is worthy of consideration. The early diarrhœa particularly should be carefully treated, as the treatment of cholera really centres in it. Therefore it would be well for the physician, as Ziemssen truly remarks, always to carry with him during a cholera epidemic the articles used in administering a tannic acid enteroclysis, so as not to lose valuable time by having to send to the druggist and to the instrument-maker for his tools. It cannot always be avoided, however, even with Cantani's tannic acid enteroclysis that some cases of choleraic diarrhœa glide into the grave attack of cholera or into the algid stage.

The diet of the patient in choleraic diarrhœa is of especial importance, particularly in the way of avoiding as much as possible everything that is injurious. Accordingly, the diet should, as a general rule, be the same that we prescribe in all processes which are accompanied by a lesion of the intestinal wall and the accumulation of deleterious schizomycetes and their poison in the intestinal canal. For breakfast milk is especially indicated, tea with cream is not so advisable; for dinner and supper oatmeal gruel, arrow root or sago soup with red wine. If the appetite is stronger, tender broiled meats may be served for dinner with mashed potatoes or boiled rice, possibly also veal or chicken ragout. Only wheat bread should be

taken, and it should be soaked when eaten. As a drink, red wine and water, or hydrochloric-acid lemonade is to be recommended. Red wine in undiluted form is as little to be recommended as other alcoholic drinks in large quantities. Alcohol indeed seems to lower the resisting-power of the body. Children should drink water or milk in which the white of several eggs has been dissolved.

Cholera Gravis.

The treatment of pronounced cholera or of its algid stage meets with far greater difficulties than that of choleraic diarrhœa. In many cases which have not yet been treated the cause of cholera, the comma bacilli, are still present in large quantities in the intestinal canal. In spite of the fact that the rice-water stools frequently continue (cases of cholera sicca with constipation are exceptional to say the least), the poison is not wholly removed. With a continued transudation going on into the intestinal canal, the comma bacilli find a favorable soil for their development, while the other forms of bacteria often disappear altogether. A copious absorption of the cholera poison takes place from the intestine or from the bacilli which have invaded the wall of the former, toxic symptoms become prominent, and among them one is found which presents special difficulties in its treatment, namely, vomiting.

A dose of medicine is administered to the patient or to subdue the intense thirst perhaps a glass of water, tea, or wine is given him. The patient gulps it down, but a few seconds later vomiting expels the fluid again from the stomach, and not only it, but also a quantity of a yellowish or brownish-colored liquid. Under these circumstances it is especially difficult to give the patient any medicine by the mouth. In many cases it is very desirable to empty the intestine by calomel or some other purgative, but the vomiting renders every attempt of this kind futile. In individual cases we may succeed in quieting the stomach by having the patient swallow small pieces of ice, in others it will become necessary to give the patient some rest by the exhibition of narcotics. A hypodermic of morphine of 0.005 gm. (gr. $\frac{1}{12}$) and over, is warmly to be recommended in these cases. It will soothe the spasm and relieve the vomiting, and what is of quite as much importance at least, will quiet the excitement and the subjective complaints. With the same object in view, the subcutaneous injection of aqueous extract of opium may also be employed.

In certain cases in which the calomel was not retained even after the subcutaneous injections of morphine, we tried to secure rest by

the administration of a solution of cocaine before giving the calomel. Now and again this was successful, but in the greater number of cases it failed, and after a short pause vomiting began anew, and the calomel which had been taken was expelled from the stomach. In these cases internal medication had to be desisted from, particularly as we are not sure it is justifiable to check the vomiting at all costs, since Alt has shown in his researches in Hitzig's clinic that morphine subcutaneously injected may be eliminated by the stomach, and since therefore it is quite possible that the cholera poison may also be eliminated by the stomach. Alt claims also that he has isolated from the vomited matter by precipitation with alcohol a body whose toxic effects he was able to demonstrate on rats and guinea-pigs. Although these findings still need corroboration, it is not surprising that the human body makes use of other channels, in case the organ which as a rule is responsible for the elimination of noxious matter from the organism fails to perform its function; for the functions of the kidneys seem to be greatly depressed in this stage of the disease. Frequently no urine at all is present or it is scanty and usually charged with albumin. The cause of this disturbance, as the experiments of Fränkel and my own have demonstrated, is due to a typical affection of the secreting elements, the epithelium of the convoluted tubules. As this disease must be looked upon as of a toxic nature, it is hardly to be expected that the kidneys should of themselves or from the effects of stimulating drugs be able to regain their normal functions and effect the elimination of the cholera toxins from the body.

Under these circumstances it seemed natural to follow along the lines laid down by nature, especially as it could not be denied that some patients seemed to do well who did not abstain from drinking in spite of their frequent vomiting, although the fluid was as a rule again thrown up. We must, to be sure, remember that these were generally robust individuals with good natural resisting-powers. Following out this line of reasoning, we have already attempted to assist the elimination and removal from the body of the poison of cholera* by gastric irrigation during the great epidemics of 1892.

The results thus obtained were not exceedingly brilliant. It may be that we expected too much for this method at that time, and ceased to continue experimentation after obtaining a small number of only slightly encouraging results. The successes obtained in the small epidemic of 1893 were very much greater, and in some cases after

* I am not able to support the views of Emmerich and Tsuboi that we are dealing with the action of nitrites in cholera intoxication. At least no methæmoglobin was met with in the blood of a large number of bodies dead with cholera, either during the autumn of 1892 or during the year 1893.

repeated irrigations even surprising. It is never safe, however, to draw definite conclusions from a few observations.

At all events, we are in possession of no positive therapeutic measures by which we can insure the elimination of the cholera poison in the algid stage. We shall therefore probably do well to employ the power of the intestine in this matter, especially as we may perhaps succeed in introducing a great amount of fluid into the former and again emptying it, according to the method of Genersich. Similar views, we know, have in part given rise to Cantani's tannic acid enteroclysis. The fact that we were by no means able to obtain the same favorable results in the algid stage as he did led to experimentation with other irrigations, as already mentioned above. However, even these did not yield any actually better results, so that we finally again returned to tannic acid enteroclysis.

In view of the experiments of Genersich, mentioned above, it might be well to try a solution of only 1:1,000 of tannic acid and to introduce larger quantities at a time, say as high as 6 or 7 litres. Should permanent tenesmus remain after several irrigations of this kind have been employed, we may follow it up by Cantani's irrigation of a one to two per cent. solution of tannic acid. Other methods of removing the poison from the body in the algid stage of cholera will have to be sought for experimentally. The end of bacteriological investigation must be especially to discover substances which enter into innocent combinations with or destroy the toxins formed in the body during an attack of cholera. If we could find such a substance, the introduction of which into the body would be safe, we might administer it by subcutaneous injection as well as by way of the intestinal canal.

Experimental bacteriology has so far furnished us with one such preparation, namely, Klebs' anticholerin. This was subcutaneously injected (6 to 7 c.c. on the first, 5 to 6 c.c. on the second day of the disease) and in so far showed an essential influence on the symptom complex that as the subnormal temperature disappeared the pallor and cyanosis of the skin in many cases gave place to its normal aspect, the pulse began to improve, and the spasm disappeared. These effects were not lasting, it is true; however, the percentage of cured was a favorable one when we regard the gravity of the cases treated, and although any influence on the comma bacilli by the anticholerin could not be demonstrated in the cases that ended with death, I would recommend a continuation and extension of similar experiments. As already mentioned above, cholera antitoxin, prepared by Kitasato, was employed a short time go by Nakagawa in Japan, in one hundred and ninety-three cases of cholera, which had been bac-

teriologically diagnosed. The mortality is said to have decreased as a result of this treatment. We are looking forward, however, to further trials of this remedy. Sequelæ of this treatment were said to have been urticaria, arthralgia, and myalgia. On the other hand it is proper to utter a warning against another experiment. Dr. Brooks, who claims to have observed a number of cholera epidemics in Memphis, has recommended the following solution as a subcutaneous injection in cholera:

℞ Sulphate of morphine	0.01	(gr. ¼)
Dilute sulphuric acid	1.0	(♏ xv.)
Distilled water	45.0	(℥ iss.)

This quantity is to be distributed in different parts of the body. Letting alone its absolute uselessness, it frequently leads to the formation of severe phlegmons. The cases of gaseous phlegmon observed by E. Fränkel were due in part to these experiments.

In addition to the intestine, the skin may also be employed as an agent in the elimination of the poison. We are not, it is true, in possession of experimental researches on the ability of the integument to excrete toxins, but the possibility of this is suggested to us by the changes of the skin in many infectious diseases, as well as by the occurrence of a cholera exanthem which is so frequently present in cases that run a favorable course in similar conditions. In order to act on the skin, we have in the first place the hot bath, which may be used with or without the addition of medicinal substances, and secondly sudorifics. Schaefer in 1831 employed the warm bath with the addition of caustic potash. The hot bath may also be of service in another way. The algid stage is accompanied, as a rule, by a subnormal temperature, as is well known. At this time the extremities become cold, the smaller arteries of the skin are contracted, the color of the skin is of a bluish-gray. It therefore seems reasonable to check for a time any further loss of heat from the body, and also to apply heat externally, and with this in view to give a warm or hot bath. We have made use of it in the algid stage with extraordinary frequency, and have increased its temperature to 35° or 36° R. (113° F.), also prolonging its duration to a quarter of an hour. The first impression produced by this hot bath is not always pleasant, it is true. Many patients, however, experience its favorable influence after a time. The feeling of oppression as well as the spasms frequently disappear in the bath, and this relief is so great that many patients after a short time asked for a repetition of the treatment. This favorable action, however, is not felt by all patients. In addition to the great number of those who immediately experience a favorable

effect, there are some in whom, although the effect on the skin in the form of reddening and dilatation of the vessels is plainly visible, the pulse does not improve and syncopal attacks exclude any idea of continuing the hot bath. Whether these symptoms should perhaps be referred to the fact that too much blood is withdrawn from the left heart and from the arterial system, by a dilatation of the integumentary vessels, I am not in a position to say. Probably the unfavorable results which Baelz has observed from the use of the hot bath, which is otherwise so much employed in the treatment of cholera in Japan, is to be referred to similar changes.

At all events, the hot bath produced a really favorable result in a large number of patients during the Hamburg epidemic. In some cases an extensive cholera exanthem followed its use, and recovery was prefaced by the disappearance of spasm, permanent loss of the bluish-gray color, and permanent improvement in the pulse. In other cases, a second or even a third bath was administered. In some cases individual symptoms disappeared, but this did not by any means prevent the pulse from again becoming weak and death from taking place, or a typical coma from making its appearance.

The effect of the hot bath may perhaps be still more heightened by the addition of mustard such as Trousseau employed in the treatment of cholera infantum. For an adult, 100 to 200 gm. (℥ iij.–vi.) of ground mustard should be made into a paste with cold water for this purpose, and this mixture, after standing a while, is squeezed into the bath through a linen bag. This bath is said to produce at first a feeling of icy cold, which is followed quickly by reaction on wrapping the patient in woollen blankets. I was not able, however, to convince myself of this feeling of cold.

We have also attempted to replace this water bath by hot-air and steam baths. But the effect seemed to be rather less than greater. In some cases, as a sequel or a substitute for the hot bath, we have also given the patient an ordinary sweat bath in his own bed by supplying hot air under the bed-clothing, the patient being allowed to breathe the air of the room. Individual patients were thrown into perspiration when at the same time small quantities of hot drinks were administered, or after an intravenous infusion of common salt. Zippel, especially, claims to have obtained favorable results from this treatment. These experiments were, however, made in a very small number of cases only and during the period when the epidemic began to decline, at which time, together with the decreasing mortality, the therapeutic results become on the whole more favorable.

In place of the hot bath, followed by packing in woollen blankets, another method has been employed by hydrotherapeutists espe-

cially. Vigorous friction is made on the surface of the skin by means of towels dipped in water at a low temperature, below 12° R. (59° F.) and continued until the skin is greatly reddened, at the same time the head is douched every two minutes with about 10 litres of cold water. Immediately after this the patient is put into a warm bed, closely covered up, a warm bottle is applied to the feet, and a compress which is renewed every half-hour is placed over the abdomen. Pure water as a drink is given the patient whenever he asks for it. If perspiration has not made its appearance by the end of three hours, friction is repeated; if it should come on earlier, six hours are allowed to pass, and then the friction is repeated for only five minutes, with water at a temperature of 14° R. (63.5° F.). During the patient's stay in bed, plenty of fresh air should be admitted to the room.

In the Hamburg epidemic, this treatment was not used to my knowledge. I myself have always been afraid to abstract still more heat from a seriously ill patient who already has a subnormal temperature. In simple choleraic diarrhœa procedures of this kind may act favorably and antagonize the cholera poison, especially by stimulating heat production and cardiac action, which, however, the hot baths accomplish equally. We may also regard as a very powerful stimulating measure the method of Casper, who places cholera patients in a warm bath at 27° R. (92° F.) and then has them douched with ice-cold water. Romberg treated twenty patients in this manner, and reported a mortality of fifty-five per cent., a result which can hardly be called an especially favorable one, and which scarcely seems to justify the enthusiasm of fanatical hydrotherapeutists.

The administration of fluids, of course, plays an important rôle in this stage. Although the loss which the body experiences from the diarrhœal stools is as a rule not so great as has been assumed at times, the thirst of the patient nevertheless goes to show the craving of the body for fluids.

As larger quantities are quickly vomited, it is advisable to administer only small quantities by the table- or teaspoonful. Hot drinks (as hot coffee or hot tea) are especially to be recommended as these are more rapidly absorbed. We would, however, do well to have regard also for the wishes of the patient, various as these may be. While we are able to quench the thirst of one with hot water, another may ask for cold water or ice. The water supplied in our ward was mainly carbonated or boiled water, to which was added muriatic acid in the proportion of 1 : 1,000. Nevertheless I do not recommend the use of water rich in carbonic-acid gas. My decided impression is that

carbonic acid acts unfavorably on the vomiting. The patients also asked much more frequently for plain water, which was first boiled and then cooled on ice. This same procedure will naturally have to be carried out wherever a drinking-water above suspicion cannot be obtained. We also replaced the latter frequently by very weak tea and coffee, but these were not received with especial marks of favor. Patients frequently receive alcohol in the form of wine or grog, and if given in small quantities this is undoubtedly harmless. Larger quantities of alcohol, however, according to my experience act rather unfavorably. The question of the patient's nourishment at this stage does not, of course, arise.

A careful examination of the pulse is to be recommended in all these cases. Frequently, with the occurrence of the algid stage, it immediately becomes small, though occasionally a notable change in the character of the pulse is noticed only some time after the appearance of the algid stage. At the same time that the pulse becomes weaker, the heart sounds also become less distinct, and the second cardiac sound frequently disappears altogether. When this symptom makes its appearance, it is only rarely that we are able to stimulate the circulation by adding heat, through the hot bath, or by hot fluids given either by the mouth or by the rectum. The subcutaneous injection of oil of camphor, which is appropriately administered repeatedly when the algid stage is threatening, will not be sufficient to make any impression after this condition is once definitely established.

The duty of the physician now consists in stimulating the heart's action by the subcutaneous or intravenous infusion of common salt solution. Which one of these methods should receive preference is not as yet decided. The dangers which were formerly ascribed to intravenous infusion are certainly not present in our modern hospitals. Intravenous infusion is undoubtedly the older of the two methods, although it seems to have been somewhat neglected in the Hamburg epidemic. In the epidemic of 1831–32 Latta of England treated 6 cases, and Mackintosh 156 cases by this method. Latta, even at that time, injected large quantities of a physiological salt solution at about the temperature of the body into different veins, and minutely described the effects which occurred. Hayem has also made use of intravenous injections in the algid stage of cholera. He used a solution containing 5 gm. of common salt and 10 gm. of pure sulphate of sodium to the litre, and injected 1½ to 2½ litres of this solution at a temperature of 38° C. (98.5° F.) into the vein at one sitting. He claims to have had good results with this method, especially when large quantities, frequently repeated in grave cases, were employed.

No injurious effects were ever noticed. Among 90 patients treated in this manner he reported 27 recoveries and 63 deaths, therefore about 20 per cent. of cures and 70 per cent. of deaths, and this in the algid stage in which alone this treatment is made use of, which furnishes, as a whole, the least chance of a favorable termination. A comparison with the total number of cases at all stages treated by other means is of course not to the point.

In the year 1866 Guttmann treated three cases with intravenous infusions, without saving a single case. The fact that some authors have inveighed against the use of intravenous infusions must probably be ascribed to these little encouraging results. In spite of this, however, we in Hamburg extensively employed this method, encouraged by the results obtained by Rieder, being emboldened to do so mainly by the introduction of the aseptic treatment of wounds, which had occurred since the time of the former experiments. To this, however, is added the fact that the opening of a vein in the algid stage of cholera, and the introduction of a cannula within it, do not present any greater difficulty than would the same operation in a dead body. I would at the same time add that any notable injury to the patient by this operation can hardly be said to have been observed.

The primary result of this infusion into the vena media or saphena is frequently in the highest degree startling; hardly have three-fourths of a litre of the solution, heated at the most to 40° C. * (104° F.), left the irrigator when the pulse of the patient rises, deep respirations occur, stupor disappears, and the grayish-blue color of the skin gives way to a more reddish tint. The patient, who has been lying in an apathetic condition all this time, may open his eyes and request a drink, and, in short, there is hardly a trace remaining of the grave picture presented in the algid stage of cholera. This favorable result is, however, not obtained in all cases in which intravenous infusion is practised. In some patients no reaction whatever is obtained; especially is there no change in the pulse and function of the heart. I have observed this by chance, when an infusion—which was heated only to 30.5° (87°) in the beginning and could only be raised to 34° (93°) by the addition of hot water—was employed, and am inclined, therefore, to attribute the chief effect of the infusion to the production of heat. I have, however, also observed a negative result in other cases, and these were exceedingly severe, perhaps complicated, cases of intoxication.

* A loss of a few degrees of heat very easily takes place as the solution passes through the tubing and the cannula.

However hopeful and startling the first result of intravenous infusion may be, it cannot be said that this will be permanent and will mark the beginning of recovery. Frequently the former condition returns within a few hours. In that case a second and later perhaps a third infusion may be given. Individual patients have in this manner received from 4 to 6 litres (in individual cases even more) of an 0.6-per-cent. salt solution, and frequently, if not always, with apparently lasting results. A great many of these seemingly saved cases, however, were taken off later by coma. In some of the wards medicinal additions were also made to the infusions (0.1 to 1.0 per cent. of thymol, hydrogen peroxide 1:1,000, alcohol), but we were unable to come to any definite conclusions as to their value. The results of the employment of intravenous infusions in the algid stage were as follows: out of 631 men 135, out of 677 women 134, and out of 163 children 50 were cured. This will furnish a percentage of 20 to 21 for men and women, for children 30, a total of 21.7 per cent. of cures. As recovery may occur even in the algid stage without the intravenous infusions (according to Griesinger in 20 per cent. of the cases), these results cannot by any means be looked upon as brilliant. They are, however, interesting in still another relation. In spite of a copious supply of fluid, in spite of temporary brilliant results, the functions of the kidneys were improved only in isolated cases, the comatose stage was seemingly not prevented, the epithelium of the convoluted tubules presented the same changes as in other cases, notwithstanding a permanently restored circulation, a result which does not support the view that inspissation of the blood is the cause of death in cholera. Therefore intravenous infusion represents only a symptomatic measure, which overcomes threatening heart failure in the same manner that tracheotomy acts in some cases of disturbances of the respiration. Intraarterial infusion, as proposed by Silbermann, was attempted in seventeen cases, among which were but three recoveries. Aside from this unfavorable final result, the technique of the method is much more difficult than that of intravenous injections (Sick).

In more recent time Gärtner and Beck, on the strength of animal experiments, have suggested the employment of a materially stronger solution of common salt in intravenous infusion, the object being to prevent exudation into the intestinal canal and the resultant inspissation of the blood. We undertook a few infusions of this kind in the small autumnal epidemic of 1893, but did not observe any more favorable results than those which followed infusions with physiological salt solution; this is still another proof that in this stage

the exudation into the intestine is less of a factor than is the poisoning of the organism.

Besides intravenous infusions, subcutaneous infusions were introduced in the treatment of cholera, especially by Cantani, although Michael in 1883 and also Samuel had previously recommended them as a result of experimental research and therapeutic study. Cantani made use of a solution which contained 4 gm. (gr. lx.) of sodium chloride, and 3 gm. (gr. xlv.) of sodium carbonate to the litre (O ij.). Of this solution, 1 to 1½ litres (O ij. to iij.) was injected at a temperature of 38° to 40° (104°) in two or three different localities, a half-litre (one pint) in each of the ileocostal or gluteal regions. According to Cantani the ileocostal regions are the most suitable localities, the pointed extremity of the cannula being directed towards the abdomen. On the whole, the skin of the abdomen is as a rule well fitted for receiving these infusions, and I would also recommend, following Cantani, that the hypodermoclysis be made in two localities at the same time. It is very easy by means of two drainage tubes to attach two cannulas and trocars to a fountain syringe. The region of the neck should be mentioned as a wholly unsuitable point for this infusion.

Cantani prefers this subcutaneous injection to intravenous infusion for a number of reasons. He insists that apart from the dangers of intravenous infusion (although these no longer exist in hospitals), the slower mingling of the blood with the salt solution is productive of better and more prolonged effects. A study of the comparative results only can settle the question, and this is extremely difficult for the reason that the individual epidemics as well as the run of cases in the various hospitals are not altogether alike as regards the severity of the disease, and furthermore, because the subcutaneous injection is practised more frequently than intravenous infusion, in the less severe cases, on account of its simplicity. This may also be the reason why Hager, after experiments conducted in Jolasse's ward in the Old General Hospital at Hamburg, prefers subcutaneous injections to intravenous infusion.

The percentage of patients permanently cured by intravenous infusion is, at all events, not so large that the method should be preferred to that of subcutaneous injection. The first would especially have to be considered in cases in which a rapid and momentary restoration of the circulation gives the only hope of saving life. In all other cases subcutaneous injection might take the place of intravenous infusion. It may also be well perhaps in certain cases to practise a small intravenous infusion until normal cardiac action is restored, and then resort later to subcutaneous injection.

The introduction of the solution into the abdominal cavity, on

the other hand, seems to me essentially more dangerous than intravenous infusion. As regards injection into the pleural cavity, I am constrained to concur in the objections against it advanced by Michael. Leaving aside the difficulty of injecting any fluid into the pleural cavity without injuring the lungs or causing pneumothorax, it also seems cruel to me to rob a cholera patient suffering from dyspnœa of a portion of respiratory surface. The use of the mucous membrane of the bladder as an absorbing surface for irrigations in cholera patients, which has also been proposed, is devoid of any theoretical or practical advantages.

That the subcutaneous injection of camphorated oil is of benefit, during the whole course of a moderate or severe case of cholera, even when heart failure is not present, need not be particularly emphasized; ether should not be employed, as the skin of these patients, being devoid of elasticity and turgescence, seems to present a tendency to necrosis, even more than the normal skin.

If the algid stage has been overcome in this manner by one or two infusions, all those measures for the removal of toxins from the body which have previously been described are again to be employed. It is especially advisable to induce perspiration in the patient by administering copious drinks. This will frequently be followed by recovery, accompanied by an outbreak of one of the cholera exanthems. The case quite as frequently, however, passes into the picture of chronic intoxication. The comatose stage (cholera typhoid) makes its appearance at times slowly, at times acutely, accompanied occasionally by fever, but more frequently by a subnormal temperature.

The Stage of Coma (Cholera Typhoid).

The results of treatment of the pronounced stadium comatosum, or cholera typhoid, up to the present time are to be considered as little encouraging. Slight cases, in which only little somnolence is present, accompanied or not by fever, frequently pursue a favorable course. The mind often becomes clear in a few days, with the advent of an exanthem distributed more or less over the body, and perfect recovery in such a case is not long in taking place. In other graver cases, recovery follows after a longer period, and thus we encounter all gradations up to the worst forms, which as a rule terminate in death, with the symptoms of paralysis of the heart or of the respiration.

It will be our duty also in these cases to endeavor, by the use of warm or hot baths of 35° (95°), or by mustard baths followed by packing in woollen blankets, or by the hot-air bath in the bed, to

bring about a derivation to the skin, and to promote sweating by copious draughts of milk and water; but the prognosis in these grave cases is unfavorable. Occasionally venesection has been practised in this stage, followed by the intravenous infusion of a physiological salt solution for the purpose of producing a dilution of the toxic substances circulating in the blood and of expediting their excretion or causing their direct elimination. The results obtained, however, have not met the expectations that were entertained. In a case of coma following cholera nostras, Rumpel poured large quantities of an alkaline fluid into the stomach through the œsophageal tube, with the object of bringing about a more rapid elimination of the poison in the body by stimulating diuresis. There would seem to be no objection to the application of this measure in cholera indica as well.

In a few cases the attempt has been made to obtain a greater excretion of urine by the exhibition of acetate of potassium, diuretin, and digitalis, and thus to promote a purification of the organism. This treatment, however, is devoid of a rational basis, as we frequently meet with a copious flow of urine in coma, or coma makes its appearance in spite of a continued sufficient excretion of urine. It is not surprising, therefore, that the administration of diuretics has been futile, and I am fully in accord with v. Ziemssen in deprecating their use. As the poison which produces coma is altogether unknown to us, we can hardly conceive for the present of any means for insuring its combination or destruction within the body. Experiments with Klebs' anticholerin have certainly given negative results in this stage. Whether any substance will ever be discovered which will act as an antidote, the future only can determine.

Complications and Sequelæ.

Under the heading of complications of cholera, the most varied acute and chronic infectious diseases are to be considered. Pneumonia and typhoid fever were the acute infectious diseases most frequently met with as complications of cholera in the Hamburg epidemic. The treatment of pneumonia is naturally to be conducted on the same lines as that of the uncomplicated disease, although a stimulating treatment is here to be pursued much more vigorously even than in true pneumonia, on account of the cardiac weakness already present, caused by the preëxisting cholera.

The complication of typhoid fever with cholera is, however, of especial interest. If the acme of both diseases should occur at the same time, the prognosis will be unfavorable. The prognosis is, however, different in those cases in which the typhoid fever is de-

veloped only after the main attack of cholera. Here the cholera bacilli may be present in the intestines together with the typhoid, without exerting any essential influence on the prognosis. We have observed two cases of complicating typhoid fever in which comma bacilli were present in the dejections for a period of six or seven days without the occurrence of any other disturbances. By the fourteenth or fifteenth day from the beginning of the typhoid fever the presence of cholera bacilli could no longer be demonstrated. Treatment in these cases will have to be essentially symptomatic. When collapse supervenes, stimulating measures, especially the subcutaneous injection of camphor, will also be in place.

Other complications of cholera, as for example tuberculosis and catarrhal pulmonary processes, valvular diseases of the heart, nervous affections, and diseases of the mind, will hardly call for any especial consideration, in view of the short duration of cholera. Affections of this kind frequently seem to remain stationary during an attack of cholera, or at any rate they are not complained of. The occurrence of a parenchymatous nephritis (Rumpf) as a sequel to cholera is exceedingly rare. The treatment of these rare cases is the same as would be that of an acute uncomplicated nephritis—namely, by milk diet, rest in bed, hot baths, etc. All remedies that stimulate the kidneys should be avoided. The prognosis is probably favorable as a rule.

A very careful treatment should be accorded to the more chronic affections of the intestines which follow cholera. These conditions, which usually run their course under the guise of a continued watery diarrhœa (the stools, as a rule, containing no comma bacilli) with total loss of appetite, leading to emaciation and extreme debility, may in weakly individuals and under unfavorable conditions lead directly to death. In other cases invalidism lasting for months is the result. This affection should therefore receive searching and careful medical supervision. These patients should be confined strictly to bed, for they do better in the warmth and rest which the bed affords. In some of our observations, at least, the prolongation and aggravation of an affection of this kind could be directly traced to the fact that the patients left the bed too soon. The choice of food must, besides, also be carefully made. Milk should have first place, and its choice has received a further theoretical recommendation lately by the discovery that it possesses the power to restrain intestinal decomposition. Patients who are not able to take milk even with the addition of small quantities of cognac may try cocoa. Besides this, oatmeal or barley gruel with red wine may be employed. As regards meat, we may begin with broiled fowl or with chopped and broiled

beef tenderloin, together with boiled potatoes or rice, but we should allow an extension of the bill of fare only very gradually. The carbohydrates, particularly bread, are to be avoided as long as possible, and so also are boiled eggs. As regards sweets, they should for a long time be used only with great care. Cases in which diarrhœa has been temporarily replaced by constipation often are benefited by rice with apple sauce. It is, however, well to allow at first only such compots as contain a large proportion of tannic acid and are at the same time easily digested. According to this blackberries are especially to be recommended. These can usually be obtained in a dried condition, but they should always be soaked for twenty-four hours in water before being prepared. After they have been soaked they can be boiled like the fresh fruit. Cranberries, which also contain tannic acid, are perhaps less suitable on account of the great number of hard seeds they contain. They may, however, be tried occasionally. A very good adjuvant to this food may also be found in a pure, light, but tart red-wine. Its percentage of tannic acid seems to exert an especially favorable influence, and from this point of view claret should be preferred to any other kind. Some Greek wines, which are very rich in tannic acid (for example, camerite), are excellent for use at this time. All wines should, however, be permitted only in small quantities. If the condition improves under proper diet and treatment, the bill of fare may be gradually extended. In most patients it is at the same time important to favor the circulation of blood in the abdominal organs as much as possible. This may be best accomplished by the use of the Priesnitz pack, which is to be employed either continually or only at night. During the day we may substitute a woollen bandage, having sponged the abdomen with a cool lotion, after removing the moist and warm pack, following this by strong friction. In the way of medicines opium or opium combined with bismuth takes the first place:

℞ Powdered opium, ... 0.015 (gr. ¼)
Bismuth subnitrate, ... 0.3 (gr. v.)
M. Sig. : One powder three times a day.

The following powder is recommended by Wunderlich:

℞ Powdered opium, ... 0.025 (gr. ss.)
Tannic acid, ... 0.05 (gr. i.)
White sugar, ... 0 5 (gr. viij.)
M. Sig. : One powder three times daily.

Bismuth alone is also frequently of great service; it should then, however, be prescribed in larger doses, these having in recent times

also been recommended by Kussmaul and Fleiner in the treatment of ulcer of the stomach. I have frequently ordered 1.5 to 3 gm. (gr. xxij.-xlv.) of bismuth subnitrate in wafers three times a day with benefit. Von Ziemssen especially recommends the bitters and aromatics, particularly those which act on intestinal digestion and peristalsis, especially if diarrhœa alternating with constipation, such as is common during convalescence, be present. First among these are preparations of rhubarb. In cases of diarrhœa in which there is much flatulence, small doses should be prescribed, perhaps in the manner recommended by von Ziemssen, a mixture of equal parts of tincture of rhubarb and compound elixir of orange being taken, teaspoonful doses twice or thrice daily. In cases of constipation von Ziemssen orders the wine of rhubarb either alone or in a mixture with compound elixir of orange and compound tincture of cinchona in teaspoonful doses. The same results may also be obtained by an infusion of rhubarb:

℞ Infusion of rhubarb, ... 120 (℥iv.)
Syrup of orange peel, ... 30 (℥i.)
M. Sig.: One teaspoonful to be taken every two hours.

Besides these, various bitter preparations, such as tinctura amara and colombo, may occasionally be employed.

We meet with some cases, however, which resist the most careful regulation of the diet and manner of living. The rumblings in the abdomen and the alternation of diarrhœa with constipation persist; the nutrition suffers and the patients are greatly disturbed in mind. In these cases, it is well to remove the patient from his present environments and place him amidst other surroundings. Von Ziemssen recommends for this purpose mud baths in not too raw mountainous regions, or in winter a sojourn in some mild climate. I have noted especially favorable results from a winter in Italy, and believe this to be due more to a favorable influence on the nervous system than to anything else. We must therefore be governed in this matter by the season of the year. A so-called mild climate, which together with a stimulating action will not put too great a strain on the heat-producing powers of the patient, is therefore to be preferred to a colder and more invigorating climate. In the North, therefore, we should prefer the hills to the sea coast, and in the cooler seasons of the year a Southern climate would again be preferable to the mountains.

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DENGUE.

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DENGUE.

Definition.—Dengue or denguis is a specific fever characterized by a peculiar eruption and arthritic pains, commencing suddenly, often remitting and liable to relapse. It attacks all ages and both sexes indiscriminately; convalescence is slow, liable to be protracted, and painful. The disease is seldom fatal in the adult. There is still some uncertainty as to whether it is contagious in the ordinary sense of the term, but that it is capable of being conveyed by human intercourse would seem to be probable. Epidemic diffusion of this disease frequently involves wide tracts of country, and occurs at considerable intervals of time, probably depending upon unknown atmospheric and cosmic conditions that favor its development, under which circumstances, Dr. Charles says, a sporadic case may sow the disease broadcast over a wide extent of country. It occurs endemically also, as for example in Calcutta, where it is known as red fever.

Synonyms.—Dengue has a variety of synonyms, classical and local, *e.g.*, Scarlatina rheumatica, Exanthesis arthrosia, Febris exanthematica articularis, and others. The local synonyms are derived from the general characters of the disease, as Dandy fever (West Indies) from the supposed stiff carriage, of which dengue itself is said by some to be a Spanish corruption, but by Corre the word is said to be of Hindoo origin; Three-day fever; Red fever (Goodeve) and Tootia (India); Breakbone fever in different parts of the world; Stiff-necked fever; Piedosa; Fièvre chinoise; Fièvre épidémique inflammatoire; Fièvre rouge exotique; Fièvre courbaturale; Bouquet; Giraffe, from the stiff way of holding the neck, and others.

Natural History and Geographical Distribution.

Dengue, like influenza, is an epidemic disease, spreading far and wide with great rapidity, involving in its incidence large tracts of country and attacking all ages and both sexes indiscriminately; yet it not infrequently manifests itself as an endemic or in the sporadic form. The area of its diffusion being chiefly confined to tropical and subtropical regions shows it to be mainly a disease of warm climates, but it may extend north of the subtropical regions. So far as our

information goes its extreme northern limits are 39° 56' N. (Philadelphia) and 36° 10' N. (south coast of Spain); or if we include certain cases which have been described by Sir B. Richardson, though their nature is doubtful, being more probably referable to scarlatina and rheumatism, the limits of the disease would be placed farther north, in the British Isles. In the Southern Hemisphere it appears to have reached as far as 23° 30' S. (San Paolo in Brazil), or if we include the few cases recorded by Ashburnham Thompson in Sydney in 1885 to 33° 54' S.

It is possible that this disease may have occurred elsewhere and have escaped recognition, and that we may in the future hear of more extended visitations both in the Northern and Southern Hemispheres. Dengue seems to have a tendency to affect the proximity of the seashore, though it has extended, as in India, over the whole continent, as far as the foot of the Himalayas.

There are accounts of the prevalence of dengue as an epidemic in the Eastern and Western Hemispheres as far back as the end of the last century. That name is not used, but the description of the symptoms is unmistakable. There are accounts of it by three different authorities as occurring in 1789 at Cairo (Gaberti), Alexandria (Marpurgo), and Batavia (Bylon). In 1780 it was observed on the Coromandel coast (Persin); there is an account of a fever in Philadelphia the same year which was doubtless dengue (Rush). Charles says that Persin had heard of it as being prevalent in Africa, Arabia, Persia, and Thibet and as having been known to occur previously from time to time on the southeast coast of Hindoostan. It seems to have prevailed epidemically in Spain in 1784, 1785, and 1786; Leblond gives an account of it in Granada towards the end of the eighteenth century, and in Lima, according to Pezet, it prevailed during the year 1818 and was very severe.

At the beginning of the nineteenth century a great epidemic of dengue occurred in the West Indies and North and South America, and from that time forward, when its chief characteristics had been fully recognized, the real history of dengue may be said to begin.

In the Eastern Hemisphere during this century extensive epidemic visitations have occurred in 1824–25, India and Further India; 1853–54, Upper India; 1870–73, the eastern coast of Africa, Arabia, Upper and Lower India, and China.

It is not easy to trace the course of the first epidemic, as the records are very scarce. Dengue would seem to have appeared simultaneously in May, 1824, in Gujerat and Rangoon; then at Chittagong and Calcutta, and subsequently at different towns up the Ganges as far as Burhampore; it prevailed at the same time at various stations

on the east coast, and in December was noticed at Cairo (Ehrenberg). In the next year it appeared at the place on the Ganges where it had stopped in 1824, prevailed in various cities farther up the river, and finally stopped at Mirzapore.

During the thirty years that elapsed before the next great epidemic of 1854, dengue was epidemic in various places: in 1835 on the Arabian coast, in 1836 and 1844 at Calcutta, in 1845 at Cairo, in 1847 at Cawnpore, in 1845 and 1848 in Senegambia, in 1851 in Réunion, and during 1852 and 1853 at Tahiti.

The chief *locale* of the second great epidemic in the East (1853–54) was Upper India, chiefly Bengal, and also Rangoon.

Then follows a second period of scattered outbreaks when dengue appeared at various places in Europe (Cadiz, 1867), Africa (Senegambia, 1856 and 1865, Tripoli, 1856, and Port Said, 1868), and also in the Canary Islands.

The most widely extended epidemic, that of 1870–73, first appeared as before mentioned in the east coast of Africa, in Zanzibar, where dengue was previously unknown, in 1870. It was not noted anywhere else that year, but in 1871 and 1872 it was at Aden, Mecca, Medina, Yeddah, and other places on the Arabian coast. At the end of the year 1871 it broke out in Port Said, Bombay, and Calcutta. During the year 1872 dengue was epidemic in the presidencies of Bengal, Bombay, and Madras and in the Northwest provinces reached as far north as Umballa and Lodiana; it appeared also in Rangoon, Upper Burmah, Shanghai, Amoy, Formosa, and Java, continuing in the last place till 1873.

In 1873 dengue was prevalent again in India, especially in the Madras Presidency and in Cochin China; Mauritius and Réunion were also attacked early in the year.

Since this great epidemic there has been no other so extensive, but only limited epidemics in various places; in Tripoli in 1878, in Port Said in 1885, and widely in Egypt in 1887. In 1889 dengue was epidemic on both sides of the Ægean Sea and in most islands of the archipelago, except Crete; in Greece (Athens), Turkey, and Asia Minor.

In the Western Hemisphere the first epidemic after 1824 occurred in Savannah in 1826. In 1827 an epidemic began which continued for two years and extended over nearly all the West Indies, the Southern United States, the northern coasts of South America, Mexico, and the Bermudas. It did not prevail in the Central and Northern States of the United States, but a few cases were reported in Philadelphia.

During the next twenty years dengue was epidemic in the Ber-

mudas in 1837, in Rio de Janeiro from 1845–49, and in New Orleans in 1849.

In 1850 there was another epidemic of dengue, widely extended throughout the Southern States of the United States; it appeared simultaneously in Savannah, Augusta, and New Orleans and spread as far south as the southern limits of Texas.

There is no extended epidemic recorded after this, but there were outbreaks at Callao and Lima in 1851, at Mobile, Ala., Cuba and other West Indian islands in 1854, Martinique in 1860, and the Bermudas in 1860 and 1863. The latest records of dengue in the Western Hemisphere are in Alabama, at Vicksburg, Miss., and at several places in eastern Louisiana, 1873, New Caledonia, 1884, Fiji, 1885, and Texas, 1885. In 1885 a few cases of dengue appeared in Sydney, all in persons who had come from Fiji, where it was then prevalent.

According to Charles and others it is never absent from some parts of India. It received the name of red fever in Calcutta, where it is most prevalent, from Goodeve who described it in 1844.

It has been believed by many, according to Maclean, that it first appeared within and was limited to the yellow-fever zone. As it has been sometimes the precursor of an epidemic of yellow fever within the precincts of this zone, there may be some grounds for this belief, but however this may be, the disease, as has been shown, occurs beyond the limits of this zone.

The official returns of the sanitary commissioner with the Government of India give the following statistics for the last ten years:

1885 European army (56,967): There were 728 cases, all in the Bengal Presidency, and no deaths. Dengue occurred in Bengal proper, in the Gangetic provinces, and in the Punjaub, the largest number of cases being in Lucknow, where the civil lines were attacked before the military. The epidemic was of a mild form and curiously enough the women and children escaped altogether. Dengue is not mentioned in the statistics of the *native troops.*

1886 European army (61,015): Dengue was only in the Bengal Presidency and in a mild form; no deaths. There were 294 cases, the largest number occurring again in Lucknow. Only three women and three children were attacked. The *native troops* escaped dengue entirely.

1887 European army (63,515): There were 120 cases with no deaths, and they occurred at four stations only: Umballa, Fyzabad, Lucknow, Yullunder. Brigade Surgeon J. A. Scott considers dengue to be endemic in Umballa and believes it to be of malarial origin, as it always appears when ague begins to prevail. The type was mild and no women and children were attacked. The *native troops* escaped.

1888 European army (68,887): There were 13 cases of dengue, with no deaths, all at Lucknow and Umballa. There was none among the *native troops*.

1889: No dengue is reported this year either in the European or native armies.

1890 European army (67,823): There was one case at Meerut and one "obscure" fatal case at Chakrata. Among the *native troops* there was no dengue.

1891 European army (67,000): There were 21 cases of dengue, 17 at Benares, 4 at Allahabad. Among the *native troops* there were no cases.

1892 European army (68,137): There were 21 cases, all at Peshawar. Among the *native troops* there was no dengue.

1893 European army (70,091): No dengue reported. Among the *native troops* there were 403 cases, all at Aden.

1894 European army (71,082): There were 42 cases, all at Aden. Among the *native troops* (127,844) there were 251 cases, 239 of them at Aden.

These statistics would seem to show that the disease is practically never absent from India, though the greater number of these cases occurred in the Gangetic provinces, while in 1893 and 1894 it seems to have prevailed to a considerable extent among the troops at Aden. It is noteworthy that in the greater number of years quoted, among the troops the Europeans alone seem to have suffered. But this exemption of natives is not general and in one year there were over four hundred cases among the native troops, and the population generally enjoys no immunity.

Most observers have remarked that prevalence is very much influenced by temperature; that dengue occurs chiefly during the hot season and when the temperature is high, and abates with a fall of temperature. In those countries where it has prevailed in which the temperature has fallen below freezing point, the epidemic has abated with the depression of temperature and finally been brought to an end with the occurrence of frost.

It may be remarked that during epidemic diffusion of this disease the proportion of the population attacked is very large. For example, in the epidemic at Lima in 1818 nearly all the 70,000 inhabitants were attacked. In 1827 at St. Thomas, almost every individual of the 12,000 was attacked; in Antigua, according to Nicholson, very few inhabitants of the town escaped. Moreau de Jonnés says that "one-half of the inhabitants of Havana were attacked *almost simultaneously.*" In Réunion in 1851 Dutroulau says it spread so rapidly that "the hospitals were crowded in a few days," and in the 1873 epi-

demic in the same colony, Cotholendy says that of the 35,000 inhabitants of the town of St. Denis about 20,000 were affected. In the epidemic of 1871 and 1872 in Calcutta, seventy-five per cent. of the population were attacked and in Madras hardly a house escaped. In Rangoon and in Formosa in 1872 about two-thirds of the population were attacked. During the Texas epidemic of 1885 Dr. McLaughlin notes that 16,000 out of the 22,000 inhabitants of Austin were attacked.

Etiology.

Many writers who have recorded their observations and experiences of dengue regard it as an infectious disease, some thinking it more so than others. The degree of communicability as well as the mode of communication can, however, hardly be regarded as a settled question. Where it occurs sporadically or as a limited endemic there is no very conclusive evidence to show that personal contact communicates the disease. Isolated cases occur in households dotted here and there over the community, without any special evidence of its spreading, and it may be that in those cases referred to by Charles where "a sporadic case may diffuse the disease far and wide," the diffusion has been due to concomitant causes of a local, cosmic, or atmospheric nature, which we are not able precisely to define, combined with defective hygiene; and it may well be that the apparent excessive contagiousness which seems to characterize many of the widely spread epidemics, in which nearly the whole population is simultaneously affected, may be due to the combination and prevalence of causes that intensify and develop the contagion which under other circumstances would show but little activity.

Though from analogy it would seem probable that such contagium does exist, and that it is of a microbial nature, bacteriological research so far has not revealed such micro-organisms, though it may well be that further research will throw light on what has been hitherto obscure.

The history of the invasion and spread of the disease would seem to point to transmission by ships and by individuals. For example, the Asiatic invasion of 1871 and 1872 appeared to have spread from Zanzibar to Aden and thence to have been carried to Bombay by two transports. Again, on the voyage of one of these vessels from Bombay to Cananore, fresh troops having embarked at Bombay in the ship which had not been thoroughly disinfected, the disease broke out among these men, who, landing at Cananore, are believed to have brought about the development and spread of the disease throughout the Indian peninsula. And again in 1872 dengue appeared at Madras

coincident with the arrival of certain pilgrims from Mecca where the disease is said to have been imported from Aden and Port Said. It is difficult, while giving due weight to general causes and other sources, to reject the possibility of this mode of transmission; and instances of the disease appearing in a healthy community soon after the advent of a person who has suffered from or been in contact with it are sufficiently numerous to emphasize the probability of its being so conveyed.

Dr. Charles, who has had much opportunity of studying dengue and who has written an admirable monograph on the subject, expresses his conviction that it is communicable, adducing examples of contact of healthy persons with the sick who were shortly after affected; but he also states that he has witnessed many instances in which isolated cases have occurred in a household without its spreading. He adds that though cases have occurred within a few hours after contact with the sick, yet the result of his observations led him to conclude that the period of incubation may extend to five days, though others have considered that it might be a few hours. He further states his belief that when the eruption is out the danger of communicability is the greatest, and that on or about the tenth day, when the eruption has disappeared and after carbolic-acid baths, the danger of communication ceases. As one prominent character of this disease is its proneness to attack the great proportion of the population of the area invaded, it must be very difficult to trace the sources of communication in individual cases, the cause, whatever it may be, being so universally distributed. At the same time it is right to remark that while Aitken, Copland, Maclean, Notter, American physicians, and others agree with Charles, yet Goodeve, Mouat, Twining, and others have considered it to be not communicable from person to person. The writer of the present article is inclined to concur with those who consider the point to be still doubtful.

The following extracts for which the author is indebted to Surgeon-Lieutenant-Colonel K. Macleod, M.D., indicate the opinions held by the medical men in India who have had to deal with the disease at a time of epidemic prevalence. They are from a series of replies to the central medical authority, furnished during the epidemic of 1871 and 1872 in India.

As regards importation, the majority trace the origin of the epidemic directly to it, a few can find no evidence of it, and fewer still look upon it as doubtful. Very fair examples of the evidence on which the theory of importation was based are the following: "Two steamers arrived (at Gowhatty in Assam) in the last week of April with several cases of dengue on board, and the first man attacked

in the station had spent several hours on board one of them the day she reached. No case appeared (in Mongyr on the Ganges) before the 5th of April and the individual then affected had but two days before returned from Calcutta. Two Eurasian gentlemen with their families also arrived from Calcutta suffering from the disease, and from their dwellings, which were in two different parts of the town, the disease gradually spread."

The medical officers who are doubtful about the evidence of importation do not as a rule assign any other origin, but the sub-assistant surgeon of Azimghur writes as follows: "There was, however, one remarkable feature in the history of the epidemic. The few scattered cases that occurred in June were all of them imported. The afflicted patients had contracted the distemper at Berhampore or Calcutta and had come home for proper nursing. They got well and did not communicate the disease to their attendants. Nor did the earlier cases occur in their households when later on dengue began to prevail epidemically. It appears as though importation *per se* was not sufficient to propagate the disease, but it required the existence and co-operation of other necessary conditions in order to develop, multiply, and spread the special virus of the malady."

Dr. Woodford, police surgeon, Calcutta, could see no evidence of importation, but "inclined to the belief that the decomposing rice which was daily being carried across the river in boats to the Howrah side was the origin of the disease."

Assistant Surgeon Keefer writes from Duryagunge, Delhi, as follows: "Nothing positive on this point (importation) can be asserted. I am more inclined to believe that the germ of the disease was transmitted by the air. Whatever the cause of its introduction, there can be little doubt but that at the time of its outbreak the temperature of the station was most favorable to its propagation—damp, rainy weather, hot and sultry by day, with a lowered temperature at night and having dews resembling the climate of Lower Bengal, in which this fever appeared to thrive, as is evidenced by its longer duration and the greater severity of its symptoms in Bengal than in the hotter and drier climate of Upper India, and also by the fact that this fever has appeared at different times in the West Indies and in parts of the Southern States of America, countries whose climate is somewhat similar to that of Bengal."

There is more diversity of opinion with regard to infection than to importation. The majority consider dengue to be very infectious (or contagious); as a rule, however, the only evidence they adduce is that if one member of a family is attacked the remainder generally suffer.

The following are a few quotations from those who doubt the infectiousness:

Dr. Meredith, medical officer of Pooree, writes as follows: "As regards its infectiousness I am not disposed to class it in the same category in that respect as small-pox or scarlet fever, which may be taken as representative infectious diseases. It pertains more in my opinion to the character of influenza as witnessed in England and elsewhere, only too frequently; where, given a certain temperature, condition of atmosphere, and a change of wind to the east, a vast number of cases break out almost at the same time in every part of a town, being severe or mild according to the state of health of the individual or the amount of protection he may possess against climatic changes. Here the resemblance between the disorders appears to stop; for if we assume that at any given time a town in England was perfectly free from influenza and when in this state we grant the accession of the above conditions, it is highly probable, if not morally certain that influenza would appear among a certain proportion of the community, even if not a single outsider be introduced suffering from it, or who had been in contact with it. While, in regard to dengue, there are at present no reasons for supposing that any known conditions of the atmosphere are apt to induce the disease *de novo;* while influenza may originate from atmospheric influences alone, it is often spread and propagated by contact; so with dengue, but in a converse manner. Now assuming that its importation into Pooree was due to contact, its rapid spread was, I think, accelerated by atmospheric conditions.

"The disease prevailed during what is termed the sickly season of the place, at the time when the rains are ceasing, the subsoil water is high, and the ground generally is well saturated and in some cases about the town for a considerable time it is perfectly water-logged. Now during this period there is every year a great deal of ague and fever at Pooree; this year dengue took the place of fever to a great extent, and curiously enough, it appeared to invest itself with some of the characteristics of the malarial disease."

Dr. Condon, civil surgeon of Cawnpore, writes: "I calculated that five out of every six members of families in which it appeared suffered from it; it did not appear to spread from house to house, but it seemed to settle down over the city for a certain time and seize upon one member after another of a family."

The sub-assistant surgeon of Agra writes: "The disease resembles in its essential characteristics the maladies generally known as epidemic, but the properties of contagiousness and an incubation period for the development of the disease can hardly be satisfactorily proved.

It appears more probable that the disease owes its origin to an endemic atmospheric influence of short duration, and the very fact of its total absence for years lends to a great extent corroborative testimony in favor of its hypothesis. The facts of a great number of persons suddenly falling under its influence and scarcely any persons of an affected locality being exempted from its attacks are also points in favor of the theory. There is no proof of any affected person having communicated it to his neighbor by direct contagion; of course his effluvia may have contaminated the atmosphere by infection."

Assistant Surgeon Goodwin, medical officer of a brigade of the royal artillery, is of opinion that dengue is eminently contagious, but writes: "Its disappearance was commensurate with the setting in of the cool, dry weather. A moist and warm state of the atmosphere was peculiarly congenial to its development and propagation; this seems to be also proved by noting the parts of the world liable to it, viz., Burmah, Madras, Calcutta, West Indies, etc., where it was much more severe than in Northern India. One fact about it is very remarkable, viz., that out of all the cases that were taken to the hill stations, there is not an instance, I believe, known of its spreading, though the stations were occupied by a community all of whom would have been susceptible to its influence, had they been a few feet lower down."

Assistant Surgeon Seaman, civil surgeon of Muttra, writes: "The only evidence obtainable on this head is the fact that the disease spread quickly through whole families and then into adjacent houses. Accurate deductions as regards infection are perhaps scarcely to be drawn from such instances during an epidemic influence. Still, the fact of the jail having escaped and having remained uninfected by the disorder throughout would appear to favor the idea that its isolation exempted it."

Up to the present time bacteriology has thrown no definite or certain light upon the etiology of this disease. Dr. Klein, for example, writes that statements have been made as to the presence in the blood of a short bacillus, but he does not consider them as satisfactory proof. Professor Wright of Netley is unable to throw any light upon the subject; Dr. Macfadyen of the Institute of Preventive Medicine, London, and Professor Crookshank of King's College state that they are not aware that any specific organism is associated with the disease. In a paper, however, by Dr. McLaughlin of Texas, an account is given of a most elaborately and carefully conducted series of experiments upon the blood of dengue patients in which he observed a micrococcus which he considered to be the specific cause of the disease. He at the same time expresses regret that he has been unable

from want of time and opportunity to pursue these investigations to their ultimate issue.

There would seem to be good reason to consider that Dr. McLaughlin has made considerable progress towards the solution of the problem, but it would be premature to speak with certainty on the subject. At least it seems probable that the time is not far distant when bacteriological research will, as in the case of other specific diseases, declare the relation of this or other micro-organisms to dengue.

Whatever its specific cause may be, as has already been shown, the origin and diffusion of the disease are conditioned by geographical position and climatic influences. That it possesses in a marked character all the features peculiar to epidemic disease is illustrated by its mode of diffusion and incidence.

SYMPTOMS.

As previously stated, dengue is an eruptive fever, considered by many to be infectious, commencing suddenly, remitting and liable to relapse, accompanied by severe pain in the head and eyeballs, swelling and pain in the muscles and joints, liable to shift suddenly from one joint to another; catarrhal symptoms with congested conjunctivæ, sore throat, swelling of the submaxillary glands, and strawberry-like tongue. A terminal rash appears about the fourth to the sixth day. Hurried respiration, temperature rising to 103° or 105° F. with a rapid pulse from 100 to 120, mark the occurrence of the initial fever and scarlatina-like rash; this appears first generally on the face, which is puffy or swollen, or it may be on the chest, back, abdomen, or knees, either as a generally suffused blush or in patches which disappear upon pressure with the finger to reappear directly the pressure is removed. This is not followed like the terminal rash by desquamation. The above symptoms endure for a period varying from twenty-four to forty-eight hours, the rash rarely lasting more than twenty-four hours; the remission lasts for a period of two, three, or four days, when the terminal rash appears which differs somewhat in character from the initial, resembling a rubeoloid or urticarial eruption, often showing itself first on the palm of the hands, and in some cases resulting in desquamation of the cuticle. This rash is sometimes so slight as to be barely perceptible, but occasionally the hyperæmia is so intense as to cause small patches of ecchymosis. It may be accompanied by a rise of temperature. These symptoms gradually subside, leaving the patient weak, exhausted, and sometimes still tortured by swelled and painful joints, especially the smaller ones.

Convalescence may be tedious, painful, and complicated by the continuance of general cachexia, with pain and swelling of the joints, enlargement of the glands, orchitis, conjunctivitis, and deafness. Remissions and relapses may continue over a period of some weeks.

In some epidemics certain phenomena are more prominently marked than in others; such are a puffy and swollen face, congested conjunctivæ, and a scarlatinal rash extending over the whole body. Diarrhœa and dysentery of a chronic and intractable character, with hepatic derangement, boils, carbuncles, and, according to Dr. Charles,

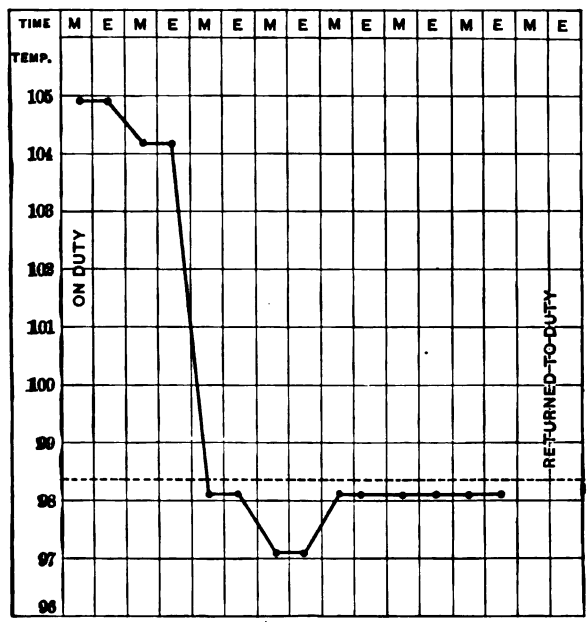

Fig. 10.—Temperature Chart in a Case of Dengue in a European Soldier, 29 years old.

insanity, sometimes complicate the disease. Uterine hemorrhage and miscarriage may also occur.

The invasion of dengue is often very sudden. The patient may have felt well up to the time of attack, the earliest symptom being severe pain in some joint, probably of the finger, which rapidly extends to other joints and bones, and during the progress of the disease is apt to pass from one joint to another. There may, however, be a period of preliminary malaise of one or more days, accompanied by anorexia, weariness, languor, chilliness sometimes amounting to rigors, giddiness, and the inaugural symptoms already described.

The symptoms vary in different cases as to the character of the rash, the temperature, and the muscular and osseous pains. The rash

may vary in color, character, and duration; it is sometimes almost absent, while in other cases it is attended with so much hyperæmia and action of the skin as to cause excessive desquamation. This hyperæmia also sometimes expresses itself in hemorrhage from the mouth and nose, the intestines, or the uterus. The fever is sometimes accompanied by delirium, or in children by convulsions, which in them occasionally initiate the disease.

Whilst there is considerable resemblance between scarlatina and dengue during the initial stage, later on the distinction becomes well marked. There is a high temperature in both at the outset, but it is

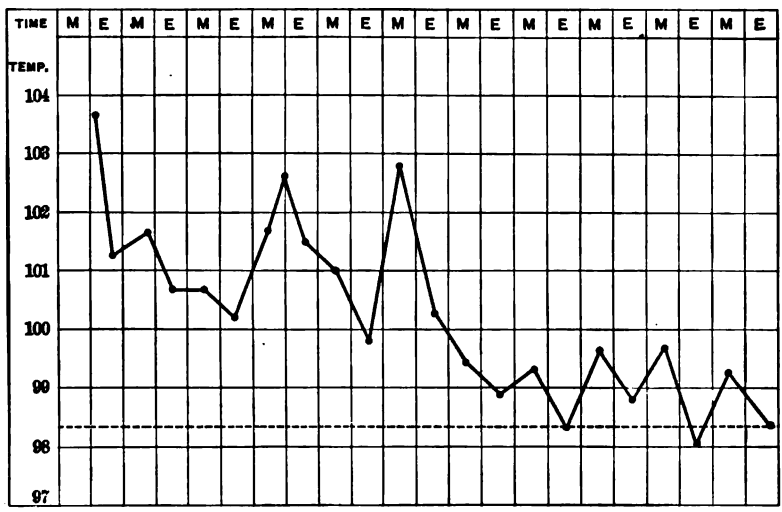

FIG. 11.—Range of Temperature during an Attack of Dengue in a Mahometan, aged 35 years. On the sixth day the terminal rash appeared, and on the seventh day inflammation at the base of the left lung was detected.

more quickly attained and more transient in dengue, while in scarlatina it endures for several days. In dengue the fastigium has a temperature of 103° up to 105° F., or upwards, but it rapidly declines and it is exceptional to find a temperature above 102° F., maintained in dengue. In scarlatina the period of decline extends over several days and is marked by evening exacerbations. In dengue the decline is rapid and the temperature may fall even below the normal standard.

The initial rash in dengue occurs sooner than in scarlatina; the pulse in scarlatina is more rapid in the early stages than is that of dengue, while the severe muscular and arthritic pains of dengue are absent in scarlatina.

Dr. Charles, who has drawn attention to the diagnostic distinction between the two diseases, points out that occasionally when the amount of poison received has been large, dengue may assume a ma-

lignant form, drowsiness may pass into coma, and the temperature may become hyperpyretic, and these with failing heart, œdematous lungs, and cyanotic surface, have given rise to the term black fever; but such forms happily are rare. On the other hand, there are very slight forms of the disease in which the patient is scarcely ill and in which the diagnosis becomes difficult; a trifling sore throat and slight malaise may be the only symptoms till the terminal rash appears to indicate what we have had to deal with, and even this may not occur.

It is considered by some that an attack of dengue, especially if the disease have run its normal course, protects the patient from a recurrence; on the other hand, authorities of equal experience assert that a first attack does not preserve from a second. There can be no doubt that many persons during the last Calcutta epidemic suffered more than once.

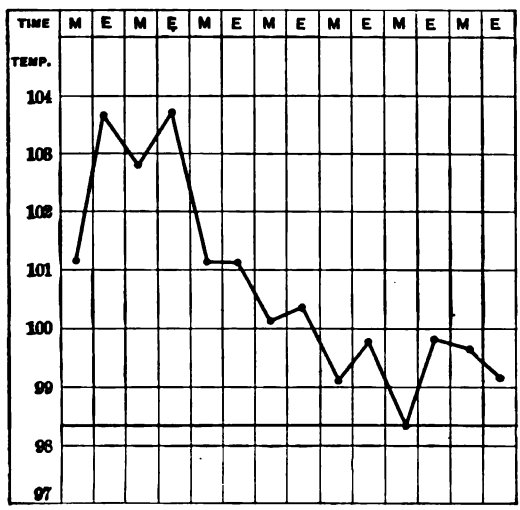

FIG. 13.—Usual Range of Temperature in Dengue occurring in an Adult European. The temperature was normal on the morning of the sixth day, although the terminal rash appeared the previous night.

The period of incubation is probably from five to six days, but it may be a day or two more or less. Relapses are frequent, and even a second or third may occur before recovery.

In simple and uncomplicated cases the average duration of the disease is about eight days, but it is frequently prolonged over weeks. While the recovery is slow and painful, complete restoration to health and vigor may not take place for months. One or other of the sequelæ already mentioned may linger, torturing the patient and retarding recovery. Albumin is occasionally present in the urine, but it is not, as in scarlatina, especially in children, so frequent or so dangerous a complication.

A few typical cases, for which the author is indebted to Surgeon-Lieutenant-Colonel Kenneth Macleod, M.D., selected from the reports of the epidemic of 1871–72 in India are here added. The temperature charts here shown are of other characteristic cases.

CASE I.—From the report of the medical officer at Umballa.

On September 24th, 1872, the wife of an inspector of police became

ill, with fever, rose-colored flush of the face and upper part of the chest, and pains in the smaller joints; the flush, though gradually fading, continued with the fever for two days. On the third and fourth days the patient was comparatively well. On the fifth day fever returned, and a measles-like eruption appeared on the face, chest, and arms; the pain in the joints continued. On the seventh day fever and rash disappeared, but the pains in the joints continued severe for about a week longer.

CASE II.—From a report by the medical officer for the Meerut circle.

An officer, aged about 32, retired on September 19th, 1872, at 9:30 P.M., feeling quite well. He awoke at 11 P.M. shivering and with ex-

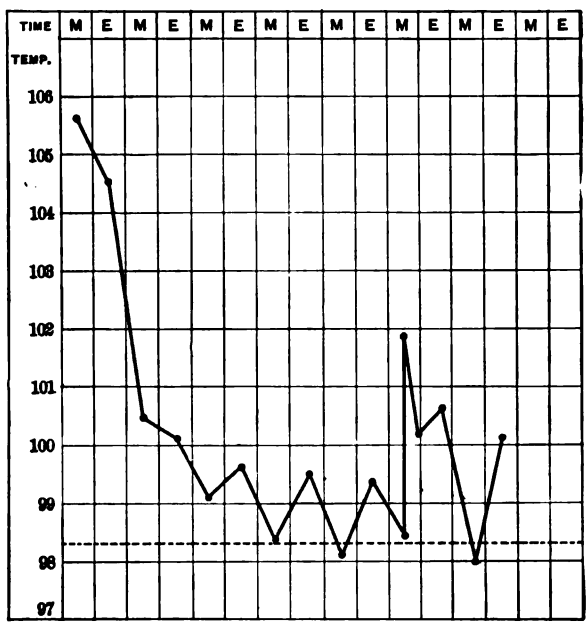

FIG. 13.—Temperature Chart in a Case of Dengue in a Brahmin, aged 16. The terminal rash appeared on the sixth day, one hundred and eighteen hours after the first seizure.

cruciating pain in feet, ankles, fingers, and wrists, as well as severe frontal headache and excessive stiffness of neck and shoulders. On the third day the pain diminished much except in one place, where it continued for weeks. On the morning of the fourth day a papular eruption came out on the hands and arms, terminating in desquamation of the cuticle. Want of appetite, disinclination for exertion, and a languid circulation remained for weeks. Ultimately complete recovery took place.

CASE III.—From the report of the civil surgeon at Lucknow.

On April 15th, 1872, a lady was seized with pains in the fingers and toes, followed by the initial rash (features swollen and eyes suffused) and fever lasting about forty-eight hours, temperature ranging from 100° to 104° F. There were great thirst, pains in the limbs and

back, and extreme wakefulness. The urine was very high colored. The lymphatic glands in the groin and axilla were swollen and painful; the general feeling of prostration and helplessness was great. After the third day some sleep and freedom from pain were obtained. On the sixth day the terminal rash appeared and gradually faded away in twelve hours; there was little or no fever or constitutional disturbance. Convalescence in this case was very protracted and the subsequent sufferings in limbs and tendons were so great that the patient had to be sent to England, where it was many months before strength and health were regained.

CASE IV.—From a report by the civil surgeon of Ranchi.

On November 29th, 1872, a child, aged 7 years, complained of

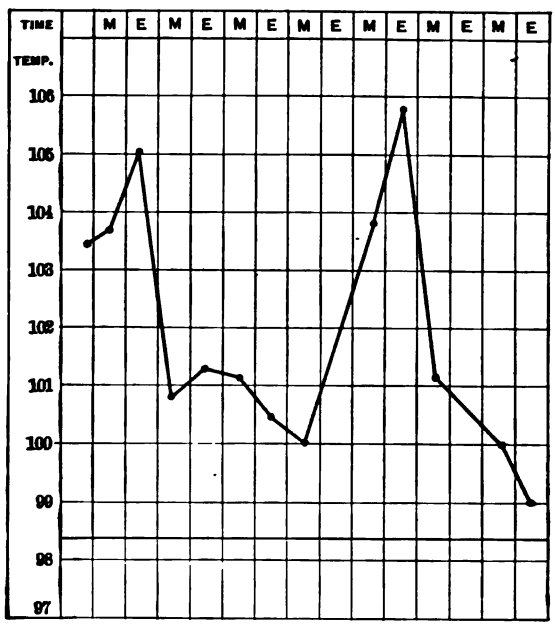

FIG. 14.—Temperature Chart in a Case of Dengue occurring in a European Child (not the one mentioned in Case IV.). The terminal rash appeared on the morning of the sixth day.

sore throat; on the 30th fever began. On December 1st this was more intense and was accompanied with vomiting and delirium during the night, but passed off in the morning. On December 2d the face was red and bloated and there was a scarlatinal rash in patches over the body, most marked on the back and inside the arms and hands; very little fever; tongue like the "strawberry tongue of scarlatina." During the night the fever again became severe. Eruption and fever were less the following day, but the throat was still sore.

December 4th, the joints and fingers of the right hand were swollen and tender; the wrists were also painful. Prostration, pain, and sore throat continued until December 9th, when the child was found to be better, and from that time began to recover.

In this case the initial rash was not observed and for some days the pains were not a marked symptom. For the first few days there was no perspiration, and afterwards perspiration and dryness of the skin alternated several times within a few hours. The state of the urine was the same as in most other febrile affections. Minute branny desquamation was observed where the efflorescence had been.

CASE V.—From a report from Dinapore by the inspector-general of hospitals.

Sepor S. R—— was admitted to hospital on August 13th, 1872, with fever and pains in various parts of the body, which was covered with a red eruption. He had felt pain in the joints of the feet and legs with headache and slight fever the evening before. On examination his skin was found to be hot and dry, the conjunctivæ were slightly suffused, pulse quick and soft, about 83, temperature 100.4° F., respiration 16; the tongue was white and furred towards the centre, red at the tip and edges, and with a few prominent papillæ; the bowels were regular, the thirst was great at times; there was headache; no appetite. On August 15th the temperature was 99.4° F., the pulse 84, respiration 14, skin hot and dry, pain still severe; urine red and less in quantity; tongue in the same condition; headache less. The following day there was no fever, but there was much pain in the knees and back; temperature 98° F.; pulse 76; respiration 16; urine of a deep yellow color, specific gravity 1.028. On August 17th the patient was convalescent; there was still slight stiffness of joints and swelling of ankles; the following day he was discharged.

CASE VI.—From the report of a medical officer in the subdivision of Serampore.

An officer went to bed at 10 P.M. feeling well though tired. He awoke at 2 A.M. with intense pain in his left wrist and by 10 A.M. he was entirely crippled, every joint being affected. The skin was very hot and felt dry and tense, headache was very severe, and there was intolerance of noise and light; great thirst, nausea, drowsiness but no sleep. The fever lasted forty-eight hours and then gradually abated, but the pains in the joints continued for two months. The secondary rash appeared on the sixth day, accompanied by a feeling of feverishness but no fever. It was very abundant on the hands and arms, and faded away in twelve hours.

PROPHYLAXIS AND TREATMENT.

In this, as in all other specific diseases, attention to hygienic measures, whether as regards prevention or treatment, is important. Thorough ventilation, isolation, and plenty of fresh air are essential. A moderate temperature of the room, exclusion of draughts and currents of air, perfect cleanliness, carefully regulated diet, and such measures as are appropriate in ordinary febrile conditions are expedient.

The treatment is simple, and if judiciously directed mitigates suffering and materially aids recovery by guiding the patient through the stages of a specific disease which has to run a certain course.

The bowels must be carefully regulated, but emetics or active purgatives are not necessary as they would increase the weakness and aggravate suffering by the muscular movements necessarily induced. Moderate action of the bowels should be brought about by bitter saline aperients combined with an occasional dose of calomel, rhubarb, or colocynth, especially if constipation exist; this is rare, though the alvine evacuations may be, and often are, dark and slimy. Saline diaphoretics, such as the acetate or citrate of ammonia, combined with liquor ammonii acetatis, or citrate of potash with nitrous ether, aconite, phenacetin, or other antipyretic remedies are desirable during the febrile condition. If the temperature reaches 105° F. or above, Dr. Charles recommends cold sponging as beneficial. The danger to life of such high temperatures, especially during the excessive heat of the hot months in India, is great, and it is then that cold sponging, affusion, or the cold bath is indicated; or the internal or hypodermic use of quinine may be of service. Belladonna seems to confer great relief; ten to fifteen drops of the tincture may be given to an adult, and two or three such doses at intervals of an hour will sometimes produce excellent effects. Equivalent doses of the extract or the juice of belladonna may be substituted for the tincture.

For the pains and nocturnal restlessness, morphine, Dover's powder, or other hypnotic may be given, while the application to the spine, back, limbs, and joints of liniments containing belladonna, opium, or chloroform may be beneficial.

All spoliative or depletive measures must be avoided, and a carefully regulated nutritious diet with stimulants, according to circumstances, must be given. Bitter vegetable tonics, such as gentian, calumba, or chiretta, with quinine, mineral acids, or dilute phosphoric acid, with which may be combined small doses of nux vomica or strychnine will prove useful. As to wine, good claret is probably the best, though others may be given if preferred. Quinine is useful rather for its tonic than antiperiodic or antipyretic effects, though when there is a tendency to relapse or when the patient is the subject of malarial taint, doses of from three to five grains may be beneficial in arresting or controlling those conditions. The bromides are recommended by some authorities, especially when nerve symptoms and insomnia are predominant, or when convulsions occur in children. Alkalies, colchicum, and other remedies in use for rheumatism have been found of very little avail in relieving the pains of dengue.

Complications such as bronchitis, pneumonia, dysentery, or hemorrhages must be treated according to the usual measures. The few cases which terminate fatally are generally due to one or other of these complications, or to convulsions in children.

The disease being one of a depressing character care must be taken, as said above, to avoid spoliative or depletive measures. The diet, though simple, must be nutritious and, when necessary, must be supplemented by the addition of wine or other alcoholic stimulant such as may seem appropriate to the particular case.

For the irritation of the skin, which is sometimes very troublesome, the application of camphorated oils or warm baths is indicated, and Dr. Charles from his large experience states that he has found them afford considerable relief.

As is the case in so many other diseases, especially such as occur among Europeans in tropical climates, complete restoration to health is promoted and expedited by change of air and climate. When cachexia and debility are severe after a prolonged attack of the disease, return to the patient's native land for a time is desirable. Care must, however, be taken to insure protection against the evil influences of moisture, cold, and alternations of temperature.

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BERIBERI.

BY

A. A. DE AZEVEDO SODRE,

RIO DE JANEIRO.

BERIBERI.

History.

BERIBERI, the kakké of Japan, is also known by other popular names in countries where it exists, the greater part of them, however, being fanciful and expressing theoretical views and erroneous opinions concerning the nature of the affection.

A disease of Asiatic origin, beriberi existed in China many years before the Christian era, being known by the popular name of *kioh-ki;* it was described two hundred years after Christ by Chinese physicians under the name of *kakké*, which was derived from two words meaning *legs* and *disease*. The word beriberi was first used in nosology by Jacobus Bontius, who in his book "De Medicina Indorum," published in 1629, describes an affection *qui ab incolis beriberi vocatur*. According to him, this word is derived from *b'hayree*, which in Hindustanee means sheep, and was used to denote a distemper that compelled the patient to walk like a sheep. Carter, who frequently observed the disease in Arabian sailors on the coast of the Red Sea, thinks the word *beriberi* is derived from two Arabic terms, *buhr*, oppression, asthma, and *bari*, maritime. The most probable etymology, however, is that proposed by Marshall and accepted by Littré and Robin, according to which beriberi is a modification of the Cingalese name of the disease *bahr-bari*, meaning extreme weakness. James Lind, in 1777, describes under the name of *barbiers* an affection observed by him with great frequency in India, and which is no other than beriberi itself. Since that time the disease has been described by various writers under the names of *barbiers* and *beriberi*, which are considered as synonymous. Marshall, in a work published in 1822 ("Note on the Medical Topography of Ceylon") established a fundamental distinction between the affections described under those denominations, regarding them as two distinct diseases. In the former (barbiers) he says paralysis and atrophy predominate; in the latter (beriberi) œdema, dropsy, and dyspnœa are more commonly met with. After this division established by Marshall and sanctioned by Copland and Scott in their classical works, the history of beriberi becomes very confused.

Malcolmson, competing for a prize offered by the Medical Board, published in 1835 an excellent essay on the history and treatment of beriberi, wherein he gave a very accurate description of the disease, describing the symptomatology and pathological anatomy. He failed to exercise any influence on the medical mind, however, and his work, which may still be consulted with profit, caused little impression, and was neglected and almost forgotten. The writers that followed him, maintaining the existing confusion, so lost themselves in conjectures and hypothetical theories concerning the nature and origin of beriberi, that from the reading of their works it would be difficult to gather any correct idea of the affection. Many diseases, especially those in which paralysis and œdema are found, were included under the denomination of beriberi. Cases of multiple alcoholic neuritis, of certain forms of diffuse myelitis, of nephritis, malarial cachexia, scorbutus, ankylostomiasis, etc., were often referred to under the name of beriberi. On the other hand, many clear cases of this latter affection have been classified as progressive anæmia, pernicious œdema, asthmatic dropsy, myelitis, malaria, infectious polyneuritis, etc.

No wonder that confusion should have reigned so long when it is seen that the disease was, according to various writers who dealt with it, characterized sometimes exclusively by motor disturbances and by atrophy, and at other times by disorders of the respiratory organs, heart, or vascular system. The diversity of opinions becomes still greater in 1861, when Fonssagrives and Le Roy de Mericourt admitted the division of beriberi in two similar but nevertheless distinct diseases. The great difference apparently existing between œdematous beriberi and atrophic beriberi justified in a measure that opinion, which was becoming more and more general and predominant. The accurate description, however, of the mixed forms and the demonstration of the relations that exist between them and the dropsical and paralytic forms, supplied the missing link between the extreme types of the disease and demonstrated its unity.

In recent years our knowledge of beriberi has been revised and enlarged. The unity and specificity of the disease have been demonstrated; the beriberi of the Dutch East Indies and of Brazil, the kakké of Japan, the barbiers of Mauritius Island, the bad sickness of Ceylon, the morbus innominatus, the *maladie des lucreries* of the Antilles, have been considered as one single affection, the same that was formerly named asthmatic dropsy and pernicious œdema. The varied and complex symptomatology of beriberi, its clinical forms, pathological anatomy, etiology, and pathogeny, have been accurately and clearly established. A well-defined place has been reserved for

it in the nosological table; and if in relation to the treatment we have not made much progress, on the other hand, from our conception of the mode of transmission of the disease, at present perfectly established, has resulted the adoption of prophylactic measures of unquestionable utility. The advances made in this new and important phase of the history of beriberi are due principally to studies and observations made in Brazil, in Japan, and in the Dutch Indies.

Definition.

Since the appearance of the works of Baelz, Scheube, Pekelharing, and Winkler, beriberi has been defined by all modern writers as a multiple neuritis of uncertain duration and extent, and described along with other forms of polyneuritis—alcoholic, plumbic, mercurial, malarial, etc. This acceptation seems too narrow and of such nature as not to render an exact idea of the disease. Notwithstanding the constant presence, as found at post-mortem examinations, of lesions of the peripheral nerves, we are convinced that the visceral disorders so frequent in the course of the disease, the injury to the nerve centres so often verified, the peculiar course with remissions and aggravations, following each other irregularly, the rapid cessation as if by magic of all the symptoms, and the prompt recovery of the patient sometimes observed with the change of latitude, the characteristic peculiar to it, among other forms of neuritis, that it may be transported to immune localities, where it constitutes permanent endemic foci, the remarkable expansion acquired by certain epidemics—all these lend to beriberi a very special feature different from that which characterizes the other forms of polyneuritis.

So, laying aside the strict and exclusive notion of a neuritis, we may define beriberi as an infectious and probably contagious disease, developing endemically or epidemically in certain localities in tropical and subtropical countries, characterized by a more or less marked motor paresis beginning in the lower extremities, always attended with partial œdemas and sensory symptoms, and sometimes with general dropsy and muscular atrophy; by visceral disorders, among which those of the lungs and heart claim special attention; by a chronic course frequently interrupted by acute exacerbations during which a rapid aggravation of the existing symptoms or the appearance of new ones takes place, when death may occur from asphyxia or cardiac syncope.

Geographical Distribution.

Considered at first as existing only on the Eastern coast of Asia, beriberi has extended little by little the circle of its geographical dominion as it has become better known. The limits drawn by Boudin and Aitken were crossed, and after the existence of the disease was made known in Oceanica, Africa, and America, the opinion of Overbeeck de Meyer was seen to be incorrect. He considered it a disease peculiar to the East, its geographical dominion being limited on the north by China and Japan, on the east by New Guinea, and on the west by the Red Sea, and on the south by the Island of Réunion. With the knowledge that we now have of the places in which beriberi has been known, we can limit the geographical distribution on the north by the 45th degree of N. lat. (the island of Yezo in Japan), and on the south by the 28th degree S. (Santa Catharina, Brazil). These two degrees of latitude bound a vast zone which cannot all be considered as the home of beriberi; nevertheless everything leads to the belief that, given certain favorable conditions, the disease once imported can develop epidemically and even become endemic in any place in this zone. The facts observed of late in Brazil, New Caledonia, and other countries prove this possibility of importation, dissemination, and permanency of beriberi in places hitherto immune. Therefore it seems reasonable and convenient to divide the great geographical zone embraced between 45° N. lat. and 28° S. lat. into two other zones: the first—zone normally beriberic—comprising the localities and countries where the disease is endemic; the second—zone accidentally beriberic—comprising the localities and countries where the disease has made one or more epidemic incursions, disappearing soon after; and those where it has never been observed, but which possess favorable climatic conditions, being susceptible therefore of invasion by the disease whenever special circumstances may occur.

Several modern writers state that beriberi, formerly so frequent in China, disappeared from that country about two centuries ago. This opinion is incorrect, and, although the disease does not seem to be so frequent in China as in Japan, yet for all that it exists and has been observed in Shanghai, Tsuchou, Wenchow, Foochow, Formosa, Amoy, Swatow, Fatshan, and Hong-Kong. In Japan kakké, considered formerly as a rare disease, acquired considerable development from the middle of the last century, and it may now be considered as one of the chief diseases of the archipelago. The greater epidemics commenced, according to Scheube, in 1740. Localized at first in the two capitals Kioto and Tokyo, it spread to several cities on the coast

and in the interior. Yokohama and Osaka are two important centres, and from Kokodate in the north as far as Nagasaki in the south all along the western coast, beriberi exists endemically.

The Dutch Indies constitute one of the most important beriberi centres. The disease is excessively frequent in Atchin, Sumatra, Borneo, Java, Labuan, Celibes, Moluccas, and the Malay Archipelago. It has not yet been observed in the Philippine Islands, but very probably it exists there. It is endemic in Tonquin, Annan, Cochin-China, Gamboge, Hué, the kingdom of Siam, the peninsula of Malacca, Singapore, and Tasmania. Less frequent on the coast of Malabar and in the Dekhan, it exists endemically in the Island of Ceylon, on the coast of Coromandel and Granjan, and in Madras. It has also been observed in Calcutta and Assam. It is prevalent on the coast of New Guinea, and has been seen in Australia, New Caledonia, and the Sandwich Islands. It is frequent in Mauritius, in Réunion, Madagascar, Nosi-bé, Zanzibar, and Aden; it has been seen in Gabun, Goréa, Congo, and Senegal.

From Asia beriberi was carried in emigrant vessels to America, and delevoped in Guadaloupe, Cuba, the Guianas, and on the Isthmus of Panama. Several writers in the United States have dealt with a peripheral neuritis occurring in fishermen on the North American coast, which is very similar to beriberi. Putnam, of Boston, in the *Journal of Nervous and Mental Disease*, mentions a limited epidemic developed on board a ship sailing from the Great Banks. The nature of that disease, however, has not been perfectly ascertained, and we cannot yet affirm it to be beriberi.

In Brazil beriberi was first diagnosed in 1866 by Dr. Patterson, an English physician, who had resided in this country many years. The first cases were observed in 1863 in the city of Bahia, and after that date the disease, which the physicians were not able at first to recognize, acquired a remarkable epidemic expansion, awakening general attention and calling forth several works on the subject. Some Brazilian writers are of opinion that before 1863 beriberi was seen in Brazil, but was not recognized. It seems beyond doubt that the disease that existed epidemically in Marianna and Diamantina, cities in the state of Minas, from 1858 to 1873, was beriberi. From Bahia it was carried to several cities on the north coast of Brazil as far as Pará, developing at first epidemically and afterwards assuming a truly endemic character. The disease broke out in Espirito Sancto, Rio de Janeiro, San Paulo, Parana, and Santa Catharina. Limited at first to the coast towns, it afterwards spread in the interior, developing in Alto Amazonas, in places very remote from the coast, in the interior of the states of Bahia, Rio de Janeiro, San Paulo, Minas,

and Matto Grosso. During the war between Brazil and Paraguay, beriberi, probably carried by recruits from Bahia, developed epidemically among the Brazilian troops encamped at Curuzú and Humaytá. In Brazil the zones of its geographical distribution may be easily mapped out. The normally beriberic zone begins in Alto Amazonas and spreads all along the coast of the Atlantic as far as Rio de Janeiro; the accidentally beriberic zone extends from Rio de Janeiro to Santa Catharina and embraces the interior of the central and northern states, with the exception of Amazonas, Pará, and Maranhão, which belong to the first zone.

In the South American countries bordering on the Pacific, beriberi is unknown.

Etiology.

The etiology and pathogeny of beriberi, notwithstanding the great attention that has been given to the subject, have not yet been established with the requisite accuracy; there are several obscure points which are problems awaiting a satisfactory solution. On the other hand the most conflicting opinions, many of which are nothing less than extravagant, have been emitted by writers on the subject, and too much importance has been given to certain etiological factors at the expense of others, all of which contributes to the already existing confusion in the minds of those who desire to know the real causes of beriberi. A close criticism of the opinions given out, and of the data furnished by observation in the several localities where the disease has been seen, is an indispensable condition for a perfect comprehension of the subject. The best method to follow in the attainment of this end would be a minute study, as complete as possible, of the conditions that attend the commencement, development, and permanency or disappearance of beriberi in collective habitations, prisons, colleges, asylums, hospitals, barracks, in famine-stricken districts, in urban civil populations, in armies on the march, and in ships on the high sea. The limits of this article would preclude a study of this sort, and we must therefore content ourselves with a statement of certain indubitable facts which have been brought out by this epidemiological study. These are: the specificity of beriberi, which can no longer fail to be considered a disease produced by a specific agent; its transmissibility, *i.e.*, the possibility of its being carried by man or objects to immune localities, and of developing there; its infectious character or the property it has of constituting permanent foci of infection in certain places.

Beriberi does not originate spontaneously in a place; it can be acquired only in localities where it exists habitually, and is observed

only in persons who live in these places or who have visited them. When it appears in a locality hitherto immune, it is because of the arrival of some beriberi patient or because objects from a beriberi centre have been brought there. When it attacks the inmates of a jail, asylum, school, etc., who have hitherto enjoyed immunity, without there being any change of climate, or diet, or any manifest alteration in the condition of life, it is because the specific agent of beriberi, its determining cause carried from a place where the disease already existed, has entered this building. When it breaks out among the crew of a vessel, it is because that vessel has sailed from, or touched at, a beriberi port, having taken on board patients or infected fomites.

From what has been said, it is to be inferred that beriberi cannot be due to meteoric influences, nor yet to a defective diet, as has often been stated; nor can it be considered as a clinical form of malaria, as was formerly held by Chinese and Japanese physicians, and as many distinguished writers in Brazil at first maintained. These opinions concerning the ultimate cause of beriberi and variants derived from them are at present totally abandoned, and are of historical interest only. The same cannot be said, however, of the opinion according to which beriberi is a consequence of helminthiasis; although not resting on a sound basis, this view has still many adherents among whom may be mentioned Erni, Kynsey, Giles, etc. James Walker, of Longside, presented to the Congress of Budapest a report comprising 887 subjects of beriberi examined at Sandakow (British North Borneo) from the point of view of the presence of intestinal parasites. Duodenal ankylostoma was found in 756 cases; tricocephalus was found in 284 cases; ascaris lumbricoides in 155; oxyuris vermicularis in 123; distoma in 2; various other parasites in 24. The ankylostoma has been chiefly blamed as the cause of the disease. A certain coincidence of geographical distribution, and the frequency with which this parasite has been found in beriberic patients in various localities, in some measure supported that opinion. The geographical distribution, however, is not precisely the same as has been vaguely asserted; in many places where ankylostomiasis is found, beriberi is not met with, and *vice versa*. The dochmius ankylostomum has been found in several countries of Europe and Africa, as Italy, Switzerland, France, Germany, Egypt, Algiers, etc., where beriberi has never been seen. Ankylostomiasis is a very frequent disease in the country, in villages and small towns in the interior. The contrary happens with beriberi. In Rio de Janeiro, ankylostomiasis, formerly frequent, is now observed almost exclusively in persons coming from the interior, or from the suburbs. Beriberi, on the contrary, known in Rio de Janeiro before 1886, has since that

time become more and more prevalent in the city. We may, however, lay aside these differences observed in the geographical distribution of the two diseases in order to confront the symptomatology and pathological anatomy of both. This comparison reveals a great dissimilarity between them, which gives rise to the belief that they do not depend on the same determining causes.

Bacteriology.

That beriberi is a disease of microbic nature, produced by the action of bacteria on the human system, cannot be doubted. The Brazilian physicians were the first to advance this theory as to the etiology of beriberi. In 1881, Pacifico Pereira, of Bahia, examining the blood of patients with beriberi, found micrococci of uniform shape and characteristics, and he asserted that there was a correlation between the presence of these parasites and the occurrence of the pathological process. On multiplying his investigations, however, he ascertained the presence of micrococci, in small number but exactly similar, in the blood of apparently healthy persons, and in that of patients suffering from other infectious disease such as typhoid fever, puerperal fever, etc. In 1883, Lacerda, of Rio de Janeiro, asserted more positively the microbic nature of beriberi. The germ, discovered in the blood and tissues of beriberi by Lacerda, presents varied forms according to the circumstances in which it is observed; its adult final shape in fresh cultures is that of a bacillus with spore formation. Under the influence of various conditions, however, we find streptococci, diplococci, or monococci; it also presents itself encapsulated or encysted. The stains for which it exhibits most affinity are methyl violet and safranin; it is not stained by methylene blue. It belongs to the aërobe class; it does not form spores at a temperature above 40° C. and grows badly under 25° C. Rabbits and monkeys inoculated with pure cultures of this bacterium presented symptoms and lesions very similar to those of beriberi. Lacerda's discovery was confirmed by Ogata Masanori and Wallace Taylor in Japan, and by Cornelissen and Suguenoya in the Dutch Indies. These observers, who were unacquainted with Lacerda's investigations, discovered in the blood and tissues of beriberi patients a microbe very similar to that formerly described by the Brazilian physician.

Later, in 1887, Pekelharing and Winkler, two careful and competent observers, undertook in Batavia and Atchin rigorous investigations on the nature of beriberi, and obtained results somewhat different from those of Lacerda. They examined the tissues prepared in

various ways and according to modern methods without being able to recognize pathogenic bacteria in them. The examination of the blood made by them furnished more positive results; they always found two species of bacteria—cocci and rods. The latter were of a somewhat irregular shape and inconstant length and thickness; they sometimes took a stain (methylene blue and fuchsin) only at the ends. Besides perfectly spherical granules, some were found of an elongated shape and others united like diplococci. The number of these microorganisms varied greatly even in the same individual. Sometimes the preparation was full of bacteria; at other times only after a prolonged examination was it possible to find a few well-determined rods or diplococci. The Dutch observers found these bacteria not only in the blood of sufferers from beriberi, but also in that of healthy persons residing in a beriberic centre, as Atchin, for instance. Examination of the blood of healthy persons in Batavia was negative; the observers failed likewise to find bacteria in the blood of beriberi subjects who had been carried from the place where they had contracted the disease to Batavia, and had been under treatment for some time. In two seamen, however, who had been landed fifteen days from the vessel on board of which they were taken ill, bacteria were found. Pekelharing and Winkler concluded that at places where beriberi is endemic, bacteria are found not only in the blood of sick but in that of healthy individuals also, and that these bacteria disappear from the blood when the sick or healthy individuals withdraw from the beriberic centre to an uncontaminated district. They remarked that in residents of Atchin, even among the apparently healthy, complaints of heaviness and pains in the legs, palpitations, and slight œdema were common; they themselves and their assistants also felt these symptoms, which disappeared only some time after their leaving Atchin. In order to ascertain which of the bacteria described acts as the ultimate factor of beriberi, the Dutch observers undertook culture experiments; they inoculated 30 culture-tubes with the blood of beriberi patients in whom the presence of bacteria had been recognized. In only 15 tubes did they obtain a culture, that in 12 of them being of micrococci, and in 3 of a bacillus. Of the cultures of micrococci 2 produced colonies of a yellow color, and 10 of a brilliant white. Of these last, 6 liquefied gelatin; with these 6 cultures they made 9 inoculation experiments on rabbits and dogs with positive results, the autopsy of the animals showing more or less extensive lesions of the nerves. One single inoculation was never followed by a satisfactory result; in order to produce an effect it was necessary to repeat the inoculations daily during many days.

Pekelharing and Winkler concluded that the white micrococcus,

liquefying gelatin, which they obtained from the blood, was the cause of beriberi. This bacterium, by the form and grouping of its cells, as well as by the aspect of its cultures on agar-agar, presented great similarity to the staphylococcus pyogenes albus; the culture on agar-agar was of a milky white color, forming a thick coat with a shining surface, and very often with indented edges; it stained readily with aniline colors in alkaline mixture, and when treated by Gram's method it was not easily decolorized. Its growth was most exuberant at the temperature of the body; at 20° C. (68° F.) it was weak, ceasing at 15° C. (59° F.). The air of barracks and places infected with beriberi contains a great quantity of bacteria. On passing this air through a neutral saline solution and inoculating this solution loaded with atmospheric microbes in animals, the Dutch investigators witnessed the appearance of symptoms and lesions of the peripheral nerves analogous to those observed in beriberi.

From the studies and experiments of Pekelharing and Winkler we may conclude:

(1) That bacteria of different shapes, sizes, and properties are always found in the blood of beriberi subjects examined at the places where they contracted the disease; (2) that cultures obtained with one of these bacteria, when inoculated in the lower animals, determined a distinct degeneration of the peripheral nerves with more or less paresis; (3) that these inoculations afford positive results only when repeated daily during many days; (4) that these pathogenic bacteria live in the soil and are carried about in the atmosphere; a salt solution, loaded with microbes contained in the air of barracks or infected places, is found to produce, when inoculated in animals, characteristic lesions. Another general conclusion results from the investigations of the Dutch savants, namely, that the infection in beriberi takes place in a very different manner from that observed in all other infectious diseases. In these, as soon as pathogenic germs enter the system and determine the disease, the latter follows its natural course independently of any new introduction of germs. In beriberi the producing germs, after living and multiplying for a certain time in the organism, die and disappear from the blood, new introductions and successive reinfections being necessary for the disease to progress.

The ingenious theory of Pekelharing and Winkler, although subject to a few objections and not based on sufficiently numerous experiments, explains satisfactorily, nevertheless, the clinical facts, and affords a good explanation of the complete disappearance of all the symptoms in many beriberi subjects who have left the district where they contracted the disease. Before Pekelharing, Brazilian physi-

cians, among whom was Lacerda, explained the aggravation of beriberi in patients remaining at the place where they contracted the disease, by the fact of accumulated infection.

The observations of the two Dutch savants were confirmed by Van Eecke, who found in the blood in beriberi two kinds of cocci, the one white, the other yellow. Rebourgeon described a micrococcus occupying the lower part of the medulla, cultures of which, inoculated in animals, produced the symptoms of beriberi. Musso and Morelli obtained from the blood in cases of beriberi, four species of microorganisms, one of which, injected in thirteen animals, produced œdema and multiple degenerative neuritis with muscular atrophy, and groups of cocci were found in the tissue of the heart.

The germs found and described by Pekelharing, Winkler, and Van Eecke are very similar to those formerly discovered by the Brazilian physicians P. Pereira and Lacerda, and it is quite possible that they are identical. Indeed, bacteria of the same shape and size, and having the same reaction to staining-agents as those found in the blood of beriberi subjects by the Dutch investigators, were observed before their time by Lacerda. The presence of micrococci in the blood of healthy individuals residing in beriberic centres was verified as early as 1881 by P. Pereira. Dealing with the same question in a more recent work, Lacerda maintains that the rods and micrococci associated with the clinical symptoms of beriberi are closely related; in the blood the micrococci predominate; but in artificial cultures the rods are more abundant and well enough developed sometimes to justify being clasified among the bacilli.

It seems somewhat premature to accept as definitive the results of the investigations thus far made concerning the ultimate cause of beriberi, for it would then be necessary to admit that the germ that produces the disease is polymorphous, and that some of the organisms found are dead and degenerate forms. Although, therefore, in the present state of our knowledge it is not possible to indicate in a positive manner and isolate the germ that produces beriberi, we must consider the disease as determined by a microorganism, whichever it be, and admit the infectious character of the affection, which, even before any bacteriological investigations were made, was established inductively by clinicians and epidemiologists.

Infection.

Numerous and evident facts have demonstrated the infectious nature of beriberi, and on this point there can be no longer any doubt. The same cannot be said, however, in relation to direct con-

tagion, which is denied by nearly all writers. It is very difficult, if not impossible, to determine this question, not only because the period of incubation of beriberi is relatively long, but also because the necessity of repeated introductions of germs in the system, in order that the disease shall develop and progress, seems demonstrated. Pekelharing and Winkler made two experiments on monkeys with negative results; in one they injected 25 c.c. of defibrinated blood taken from a beriberic suffering with dyspnœa; in the other they introduced under the skin of the thigh a piece of the popliteal nerve taken from a beriberic who had died a few hours before. It may be objected in this case that the disease did not develop in these animals for the reason that there was only one introduction of germs, in the same manner that it does not develop when one single inoculation of micrococcus cultures is made.

It has been alleged against the direct contagion of beriberi that the disease does not spread in hospitals among other patients, when cases of beriberi are admitted, that it does not attack nurses, visitors, and members of the same family, and that it has not yet been observed in persons visiting localities where it prevails, unless they remain there for some time. As to visitors, that is, persons who have been in transit at the infected places or who have approached a patient, it may be objected that the disease develops only after successive introductions of germs in the system. Nevertheless, instances of the transmission of beriberi to other patients in hospitals are not so rare and exceptional as has been affirmed. Grall, Porée, and Vincent in a work on beriberi in New Caledonia, published in the *Archives de Médecine Navale*, 1894, state that in a patient affected with chronic gastritis under treatment in a hospital where there had been beriberi patients, the first symptoms of the disease appeared at the end of a month and a half. Facts of this nature have been often observed in Brazil. In Rio de Janeiro, for example, the first persons who contracted beriberi in the city were sailors and soldiers who had been in the military hospitals, where persons having come from the north of Brazil affected with beriberi were under treatment. Instances of the development of beriberi in jails, schools, asylums, hospitals, barracks, ships, etc., after the admission of contaminated persons are sufficiently numerous and well known to render useless any special citation. In an article published in the *Revue Médicale de l'Est* (1896), Dr. Hagen relates several facts tending to demonstrate the evident contagion of beriberi imported by a shipload of Indo-Chinese prisoners into New Caledonia, which, until the arrival of the ship *Cheribon*, in 1891, had always been immune. These cases, as well as those already referred to, are not of a nature to

demonstrate the direct contagion of beriberi, since the germ of the disease brought in the body or in the clothes of the patient might contaminate the soil and constitute a centre of infection.

There is, however, another order of facts that merits attention; it is the permanence often observed of the disease in a collective dwelling, notwithstanding the removal of the patients and rigorous disinfection. Beriberi developed in Rio de Janeiro in the Blind Asylum, which is a fine new building solidly constructed, with large and well-ventilated accommodations, having all hygienic improvements, and with a capacity for ten times the number of inmates that it possesses. The director of the establishment, who was a distinguished physician, used every effort to extinguish the epidemic; he improved the food, ordered all the patients to be withdrawn from the building, and had it thoroughly disinfected, but in spite of all this the disease continued, the director himself and members of his family falling ill of it. In 1893 the Brazilian Government appointed a committee of physicians, of which I was a member, to study the causes that determined the permanence of beriberi in this institution and means of removing it. The committee recognized that the general hygienic conditions of the building were the best possible, that there was no excess of inmates, that the water could not be suspected of contamination, since it came directly from the pipes destined for the supply of the city; that the food was good; that irreproachable cleanliness prevailed in all the building and its dependencies; they proposed the withdrawing of all the patients, and advised a rigorous disinfection, according to modern methods, of clothes and other objects, and of the walls, floors, doors, etc., of the whole building and its dependencies. Notwithstanding the withdrawal of the patients and the disinfection, the disease continued and still continues to be observed, and it is a fact worthy of note that it is almost exclusively limited to the female department. It is possible that some germs may have resisted the disinfection or were not reached by the antiseptics; it is also possible that some inmate, in whom the disease was in a state of incubation, may have fallen ill afterwards and transmitted it to the others.

The cruiser *Benjamin Constant* of the Brazilian navy, a new vessel in the construction of which were observed all the precepts of modern hygiene, left the port of Rio de Janeiro last year on a voyage of instruction. She navigated by sail for some time along the southern coast of Brazil; she afterwards went north and was stationed at Pará. During all this long voyage no case of beriberi was observed; on leaving Pará, where the ship was anchored about one month, and where beriberi prevails endemically, the disease broke out on board

and attacked more than fifty seamen one after the other. On arriving at Bahia the commander put all the patients ashore, and ordered a strict disinfection of the vessel; in spite of this, the disease continued to be observed, but on a smaller scale; from Bahia the vessel went to the Lazareto of Ilha Grande, where she was completely disinfected, but the disease did not cease entirely.

On the other hand, it often happens that beriberi, after its epidemic paroxysm, disappears from a place never to return, and this without any hygienic measures whatever being put in practice. This seems to show that the germ producing the disease did not find in the soil conditions so favorable as those which exist in endemic centres, unless we admit the possibility of its having lost its virulence and living there as a common saprophyte. In the seminaries of Caraça and Marianna, in the city of Diamantina, in the states of Santa Catharina and Paraná, in the city of São Paulo, and in other localities, beriberi, after having developed epidemically, disappeared and has never since been seen, and this without the employment of any prophylactic measures.

Patrick Manson says that he has never heard of a medical man being attacked, but in Brazil scores of physicians have been attacked with beriberi and have died in consequence.

Nothing that has been said above proves direct contagion, which, as I have said before, is very difficult, if not impossible, to demonstrate. Beriberi is evidently not a contagious disease in the same sense as syphilis, rabies, and smallpox, and the other acute exanthemata. True parasites, such as are the germs of these diseases, are not accommodated to other surroundings and can complete the various stages of their existence only within the human body. Nor can beriberi be compared to malaria, as has been done so often; Laveran's hæmatozoon cannot live or multiply in the interior of houses, in floors or walls; it does not adhere to objects in daily use, to clothes, or to the human body, so as to be carried to immune places and there determine the eruption of the disease. A better and more substantial analogy seems to exist between beriberi and the so-called infectiocontagious diseases, such as typhoid fever, yellow fever, dysentery, pneumonia, etc., which, having their origin usually in infection and only developing in individuals who frequent contaminated places, may under certain circumstances be propagated by contagion. In these diseases contagion is a contingent property, subordinated in its manifestations to variations in the energy of the virus and in the predisposition of the individual. That is why they are, like beriberi, strongly influenced in their endemic character and in their epidemic expansion by atmospheric vicissitudes, by climate, by

crowding, by improper food, and by other causes that weaken the system.

The question of contagion is in some measure theoretical and speculative; the practical notion that we should attempt to establish is that of transmissibility, either by infection of the soil, contamination of the air, water, or milk, or by direct or indirect contagion. In this particular there can no longer be any doubt; beriberi is a transmissible disease, and has already been considered as such by the governments of Brazil, Uruguay, and the Argentine Republic, and in the sanitary regulations of this last country it figures among the diseases subject to compulsory notification along with yellow fever, cholera, plague, etc.

Our knowledge of the beriberi-producing germs is yet too rudimentary for us to form a certain opinion concerning its conditions of life, the circumstances that facilitate or render difficult its multiplication outside of the system, and the manner in which it enters the human body. Everything leads us to believe, however, that it lives in the soil and in the interior of dwellings, being carried from one place to another by the atmosphere. Observations made in several localities show that the poison of beriberi is not introduced in the human body by food or water. The influence of the soil on the constitution of endemic centres is preponderant, since we see beriberi fix itself with remarkable predilection in certain places, but disappear spontaneously from others subject to the same conditions of climate. We do not know what are the elements indispensable for the soil in order that it may constitute a ground favorable to the life and multiplication of the beriberi germ. It has been held that it prefers swampy and damp lands, the neighborhood of the sea coast and the shores of rivers. Nothing is less true; for beriberi has been seen in places where the soil is of a constitution and nature the most varied possible. In Brazil it is frequent on the shores of the rivers in the state of Amazonas, and in the seacoast towns; but it is likewise endemic in the cities in the western part of the state of São Paulo, many leagues from the coast; and it has been observed in many places that are free of malaria and the soil of which, being of a volcanic nature, is not apt to constitute a ground favorable to the development of malarial fevers. It is possible that the contamination of the soil by animal matters favors the life and multiplication of the germs. It is very probable that this contamination renders the soil and surroundings of prisons, schools, asylums, etc., exceedingly liable to beriberi inoculation. Impure air, determined by overcrowding in confined places, must likewise favor the development of beriberi, and, when once developed, contribute to its rapid spread. The mephitism of the soil and

air, however, cannot of itself generate beriberi; it only renders the soil and surroundings favorable to the life and multiplication of the specific germs.

Meteorological Conditions.

Frankly a disease of the seasons in Japan and in all the subtropical zone, developing all the year but with summer and autumn paroxysms in localities lying between the tropics, beriberi is certainly influenced in its outset by meteorological conditions. Little is positively known in relation to the manner in which these act, nor is it known which of the meteorological elements exercise the greatest influence. It appears to be established, however, that humidity and high temperature are necessary for the disease to break out. These two conditions are always observed in all beriberi centres. The following fact likewise confirms the etiological influence of heat and damp; in Brazil in localities lying very far from the coast and at a great altitude, and which, notwithstanding their situation between the tropics, have a relatively low mean annual temperature and well-marked seasons, beriberi acquires a periodical character, the first cases appearing at the end of summer, which is the time of the great heat and wet weather, and disappearing in winter and spring.

Predisposing Causes.

Not all those who frequent a beriberi centre are attacked, and in epidemic periods many are spared. This indicates that the presence of the beriberic poison in the blood is not a sufficient reason for the person to fall ill; there must be the concourse of certain factors capable of creating a condition of predisposition, by diminishing the resistance that the human system opposes to the action of the germs. Various circumstances operate in the way of exaggerating the morbid receptivity for beriberi.

Age.—General observation shows that beriberi is excessively rare in infancy and childhood and in old age. In the epidemic that broke out on board the ship *Indien* all persons under fifteen years were spared, there being fifty-six on board. Fifty-five children took passage on board the *Jacques Cœur* and none of them presented the symptoms of beriberi, which decimated the crew of that vessel. In the seminary of Caraça, state of Minas, Brazil, beriberi attacked the pupils over fifteen years old, but spared their roommates under that age. In the years 1889 and 1890 the number of deaths from beriberi in Rio de Janeiro was 830; of these 2 were of persons between one and seven years of age; 11 between eight and fifteen years; 466 between

fifteen and thirty-five years; 285 between thirty-five and fifty years; 57 over fifty years of age; age unknown, 9. The most susceptible period of life seems to be between the age of sixteen and thirty-five.

Sex.—Statistics show that women are less predisposed than men. In Japan, according to Corre, the proportion of females to males affected is 1 to 27. Dr. Tokaki and other Japanese physicians think this difference is entirely a matter of diet. In 1889 and 1890 beriberi caused 830 deaths in Rio de Janeiro, 720 being in men and 110 in women. This great difference is explained by the fact that the disease develops in preference among sailors and soldiers. All Brazilian physicians are agreed that, in the civil population, beriberi attacks men and women almost equally. The proportion given by Silva Lima of 28 males to 22 females is perfectly correct.

Race.—No race enjoys immunity from beriberi. In Japan and the Dutch Indies the Europeans were spared during many years, and from this fact it was inferred that the Caucasian race was immune; it was discovered later that whenever they were exposed to the causes of the disease, they acquired it. In Brazil, beriberi attacks all races, the black, however, being less susceptible.

Occupation.—Persons leading a sedentary life, inmates of jails, asylums, and schools, sailors, soldiers, and laborers working in damp and ill-ventilated places are the most predisposed to the action of the beriberi poison.

State of Nutrition.—Overbeeck de Meyer observed in the penitentiary of Batavia a marked predilection of beriberi for muscular and robust persons. Patrick Manson says: "It is a singular fact, and one contrary to what obtains in many other diseases, that the robust and well-nourished seem to be more liable to beriberi than the feeble and half-starved." Further on he adds: "My own impression is that beriberi attacks any one irrespective of his physical condition, just as measles and smallpox do." Observation in Brazil confirms this last opinion, showing that beriberi attacks indifferently persons of all constitutions and temperaments.

Defective Diet.—It was long believed that feeding exercised a positive influence as a predisposing, and even as an exciting cause of beriberi. Overbeeck de Meyer, J. Rochard, Le Roy de Mericourt, Masé, and others maintained that the disease was due to deficient and bad food. In Japan beriberi is now considered a disease caused by defective feeding. Dr. Kanahiro Takaki, late director-general of the Tokyo Naval Hospital, attributes the disease solely to errors in diet, believing the cause to be an improper proportion of carbon and nitrogen in the dietary, which instead of being as 1 N to 15 C, he found invariably in all outbreaks he inquired into in civil life, in the

army, in jails, and in the navy, to be as 1 N to 22 C. This excess of carbon so alters the composition of the blood as to induce or cause beriberi, and so sure is he that his opinion is correct that he affirms that, given a hundred healthy individuals, he could by diet alone produce beriberi in them in six months, or given a hundred recovered cases, he could prevent a relapse by diet alone (Bentley). Dr. C. Aoki also, in a recent work, attributes kakké to errors in diet, consisting of an excess of carbon. Acting according to these ideas the Japanese Government modified the rations of seamen in 1884, and after that date beriberi, which had caused enormous ravages every year in the imperial navy, disappeared almost completely. In 1883, with an effective force of 5,349 seamen, there were 1,236 cases of beriberi; in 1886, with an effective force of 8,475 seamen, there were only 3 cases. It should be remembered that when the Japanese Government modified the food of the sailors it improved at the same time the ventilation of the vessels, rendered them drier and cleaner, and instituted other hygienic improvements. As early as in 1878, Van Leent and Gayet had found that improvement in the rations of the natives in prisons and on board ships, either alone or combined with other hygienic measures, was sufficient to reduce greatly the proportion of patients in prisons and to stop the epidemics on shipboard. Notwithstanding these facts, which contribute to strengthen still more the opinion of the Japanese physicians, beriberi cannot be admitted to be an intoxication of alimentary origin, caused by nitrogen starvation. The Brazilian observers demonstrated that beriberi attacks indifferently rich and poor, well-fed persons enjoying every comfort, as well as those who are subject to all sorts of privations. When beriberi develops in the civil population it even shows a certain predilection for the higher class of society. Brazilian sailors all receive equal rations of food; nevertheless beriberi develops among the crews of some ships while it spares others. The same may be said in relation to the Brazilian army. In view of these facts it is wholly impossible to admit that beriberi is due to errors in diet.

Pregnancy and the Puerperal State.—Many observers have remarked the susceptibility of pregnant women to beriberi, and the facility and frequency with which the disease develops during the puerperal period. Bentley says: "A very peculiar fact, and one which I am quite unable to account for, is the susceptibility of women after childbirth to be attacked with beriberi." Silva Lima in 51 cases of beriberi found 23 women, of whom 10 were in a puerperal condition. This learned observer says, with a good deal of reason: "The most remarkable inference to be drawn from these

statistical data is that the puerperal state is one of the most frequent predispositions to the paralytic form of the disease." In 175 cases Pacifico Pereira found 52 women, of whom 31 were in the puerperal condition.

Former Diseases. Latent Neuritis.—Beriberi is observed with relative frequency in tuberculous and syphilitic patients, in convalescents from smallpox, measles, scarlet fever, scurvy, typhoid fever, and dysentery. According to Corre, inveterate drinkers are greatly predisposed to contract the disease. In Brazil it is frequently observed in persons suffering from malarial fever; in thirty-nine beriberics Torres Homem found twenty-one who had formerly had malarial fever.

This remarkable predilection of beriberi for the stage of convalescence in infectious diseases cannot be explained merely by the weakening of the system, anæmia, and disturbance of general nutrition then observed, for beriberi is rare and exceptional in chlorotics, in leucocythæmic and anæmic persons, and in those weakened by other causes. Nina Rodrigues, of Bahia, who studied this question carefully, admits that the existence of a latent neuritis, similar to that which Pitres and Vaillard found in tuberculosis and typhoid fever, excites a real predisposition to the intercurrent manifestation of beriberi. In support of this opinion he presented statistics, which agree perfectly with others collected by Scheube, relating to the most frequent complications of this disease. The stage of convalescence from acute infectious diseases being precisely the period of polyneuritis, no wonder that beriberi is frequent at this time, since, owing to the existence of a latent neuritis, the nervous system becomes more vulnerable. Furthermore the hypothesis of a latent neuritis explains satisfactorily the frequency of beriberi in inebriates, in women in the puerperal state, and even in persons who have formerly suffered from beriberi. It is a fact of general observation that previous attacks render the individual predisposed to a relapse after a fresh exposure of even brief duration to the influences of a beriberic centre.

The Incubation Period.

The duration of the period of incubation of beriberi has not yet been determined with precision. It was long believed that a residence of several months and even of two years in a contaminated place was necessary for the disease to declare itself. Recent observations in the Dutch Indies and Brazil have shown that beriberi may develop in individuals coming from an uninfected locality, four or five weeks after their arrival in a beriberic centre. It is difficult to establish the

duration of the incubation period, as the beginning of the disease often passes without being noticed by the patient himself. It seems certain, however, that the time elapsing from the first exposure to the beriberic poison to the full development of the disease will depend on the degree of virulence of the germs, the continuousness with which they are absorbed, and the individual idiosyncrasy.

Symptoms.

The symptomatology of beriberi is varied and complex; few diseases present such diverse clinical features, hence the difficulty in diagnosis met with by those who have never observed it. This difficulty increases when the inexperienced physician or student allows himself to be guided by certain descriptions the authors of which attach too much importance to some symptom or clinical syndrome always considered predominant, and which may, nevertheless, be wanting. An accurate and complete description representing a faithful picture of the disease is extremely difficult, if not impossible, because of the complexity of the symptoms, their instability, and the different clinical features beriberi may present. To form an approximate idea of the complexity of the symptoms and their apparently inexplicable and confused grouping, it is enough to bear in mind that the symptomatology must vary according to the nerves implicated, and that the latter are not always attacked in the same order and with the same intensity; that the beriberic neuritis may be more or less extensive and intense; that it attacks some nerves or groups of nerves while it spares others; that the nerves first affected may regenerate, and that those spared may be subsequently implicated; that among the nerves affected there are found motor, sensory, and vasomotor nerves and others presiding over the functions of the organs essential to life such as the heart, the lungs, etc. Notwithstanding the great variety of symptoms beriberi is easily recognized by experienced persons who have had opportunities to observe many cases, and in endemic centres, like Brazil for instance, physicians frequently diagnose the disease at a distance.

Almost all observers have described prodromic symptoms of beriberi, symptoms which, according to the microbic conception of the disease, ought to correspond to the period of incubation. Oudenhoven and Malcolmson say that chill and headache exist; Torres Homem, Silva Lima, and others assert that the disease is preceded in many cases by a feeling of sadness, presentiments, incapacity for work, muscular fatigue after the slightest exercise, breathlessness, insomnia, the patient being tormented by bad dreams and nightmares

during the few moments of sleep enjoyed, anorexia, and sometimes palpitations. Manson says that in most cases the development of the more pronounced features of beriberi is preceded by certain vague and ill-defined symptoms, which may be considered to constitute the prodromic stage. For several days or weeks the patient finds that he is not quite up to his work; he is languid, his legs and knees feel weak, he is easily put out of breath, he has vague pains in the calves of his legs, sometimes he has headache or feels chilly, and he is easily exhausted by mental as well as by physical effort. Now and again for a few days the patient may feel quite well, but presently he relapses and he may keep getting better and worse in this way for a considerable time before the more characteristic symptoms of the disease definitely declare themselves.

All these symptoms described by writers as constituting the prodromic stage cannot, however, and should not, be considered as such, for when the patient complains of them the disease is already established and in its full stage of evolution; they indicate that beriberic neuritis already exists, and on examining directly at this time certain nerves and muscles, we shall find well-advanced alterations in them. Besides, by the analysis of the symptoms observed at this so-called prodromic period, we may often diagnose beriberi with some accuracy. The merit of having called the attention of the profession to this fact belongs unquestionably to Pekelharing and Winkler. They demonstrated that in the cases of hyperacute or galloping beriberi, the patients complained during days and weeks of those symptoms preceding the sudden appearance of serious disorders, and if during this initial phase we should examine carefully by means of electricity some of the nerves and muscles we should verify the existence of well-advanced alterations, which proves that every so-called hyperacute beriberi has a relatively long duration. They afterwards studied systematically the initial symptoms of beriberi and observed them in all the clinical forms of the disease. I myself have had numerous opportunities of verifying the truth of the facts noted by the Dutch savants, and I believe that, in the study of the symptomatology of beriberi, it is no longer reasonable not to admit and describe an *initial stage* which often passes unnoticed by the patient, during which he complains of vague symptoms, but which can be recognized by experienced physicians who will make an accurate and minute examination.

During the initial phase the patient complains of inaptitude for work both physical and intellectual; he feels tired and pants after the least exercise; sometimes he mentions cramps in his legs; often, however, he complains of a feeling of heaviness in the legs together

with slight numbness and some weakness. According to Dr. Alfredo Britto, the patient experiences great difficulty in squatting and greater still in rising suddenly after having remained in a squatting posture for some time. Many patients call the physician's attention to the heart; they feel troublesome and frequent palpitations, which come on either spontaneously or after the slightest exercise; the examination of the heart may then reveal accentuation of the pulmonary second sound and a slight increase in dulness over the right heart. Others complain of symptoms of gastric embarrassment with loss of appetite and continuous nausea and occasional vomiting. Not infrequently the practitioner is called to see a patient suffering from fever of an intermittent or remittent type attended with coated tongue, nausea, anorexia, and sometimes vomiting. The practitioner supposes he has a case of malarial or gastric fever, and treats his patient accordingly; the latter, however, fails to improve; the fever continues for ten days or more; then comes on either dyspnœa, or incessant vomiting, or serious cardiac disturbance, and the patient dies. At other times, at the end of ten days or more, the fever ceases and the appetite returns, but the characteristic symptoms of beriberi which then appear facilitate the diagnosis. In almost all patients there is a peculiar puffiness of the face, which gives them a particular and characteristic expression, by which, not infrequently, it is possible to recognize beriberi. On examining the legs we find a slight œdema, elastic and hard, which does not retain the impression of the finger, extending along the edge of the tibia. When the practitioner squeezes the muscles of the calves the patient complains of pain. The examination of cutaneous sensibility reveals a widening of the tactile zones. Wernich claims to have always found on the ankles an ordinarily well circumscribed area, where slight impressions are not felt. Pekelharing and Winkler described, among the first symptoms of beriberi, an increase in the diameter of the tactile zones, observed chiefly in the lower extremities; I have had many opportunities to verify and confirm this fact, and I consider the symptom as one of the earliest in beriberi. The most important symptoms in the initial stage of beriberi are revealed by the electrical examination of the muscles and nerves; there is a diminution of the irritability of the muscles, both direct and indirect, for the faradic current; there is at the same time a considerable diminution in the indirect muscular irritability for the galvanic current, and still greater diminution in the direct irritability; besides this, there is sometimes a somewhat slow contraction, which always takes place with both anodal and cathodal closing. These phenomena prevail chiefly in the peroneal and tibial nerves and in the muscles governed by them.

They should be considered in some measure as a partial and particular reaction of degeneration, and also as a simple quantitative diminution of the direct and indirect irritability of the muscles for the two kinds of currents. The symptoms in the initial stage of beriberi augment little by little; the disease commences insidiously and goes on increasing in geometrical progression, frequently without the patient suspecting it, until an acute exacerbation accompanied in some cases by fever forces the knowledge on the patient and his physician that his condition is serious. At other times symptoms persist during weeks and months, subject to alteration of improvement and aggravation; during the remission, the patient may feel very well for a few days and even attend to his customary business. It is in these cases that are sometimes observed sudden cardiac symptoms, acute and considerable dilatation of the right cavities of the heart, soon accompanied by asystole, death occurring either in a few days or suddenly. These symptoms may be preceded immediately by gastric crises similar to those of tabes. At other times rapid and severe dyspnœa threatens the life of the patient who may die from suffocation. Acute dropsy of the pericardium and œdema of the lungs are also sometimes observed at the end of the initial stage, as well as during the subsequent course of the disease.

Motor Disturbances.—In most cases the transition between the initial phase and the declared stage of beriberi takes place slowly and gradually; to the vague and ill-defined symptoms of the initial phase are added others, which denote that the nerves of voluntary motion and those of general sensibility are involved. The weakness of the legs, which at first the patient felt only when walking fast or going upstairs, becomes more accentuated and constant, and is accompanied by a feeling of heaviness; the patient walks slowly and often feels that his legs are about to fail him, bending and not obeying the action of the will. These troubles are soon followed by other graver ones which constitute beriberic akinesia. This is a more or less intense paresis, always beginning in the lower members and rather choosing the extensor muscles; the anterior tibial, the extensor of the great toe, and the common extensor of the toes are sometimes almost entirely paralyzed. At first incomplete and limited, the paresis becomes more and more pronounced, acquiring greater intensity and invading a greater number of muscles; it usually travels progressively upwards; after the muscles of the legs, those of the thighs are affected, and then those of the forearms, arms, and hands, abdomen, and thorax. In the upper extremities there is also a certain predilection for the extensor muscles, so that we sometimes see the peculiar distribution noted in the various types of lead palsy. As

the disease progresses, all the muscles of the extremities become affected, including those of the fingers and the interossei. Paralysis of the sternocleidomastoid and trapezius has not yet been observed; Pekelharing believes that the biceps and great pectoral are among the last to be attacked; the facial muscles and the extrinsic muscles of the eye are sometimes, though rarely, involved. Those of the larynx are more frequently implicated; hoarseness is observed in many cases, and this, according to Van Eecke, is due not to the paralysis of a definite muscle or physiological group of muscles, but to paresis of all the muscles. Pekelharing and Winkler believe that the paralysis of the larynx may be the cause of sudden death.

Seldom is a complete motor paralysis observed; in a sitting or reclining posture, even in the advanced stages of the disease, the patient is still able to move the paralyzed members. When the disease, after having reached a certain period, tends towards a cure, the akinesia retrogrades also in a gradual manner, following a descending course. It first abandons the muscles of the thorax, then those of the abdomen and those of the upper extremities, and finally those of the lower limbs. This fact, as well as the ascending progressive evolution at the beginning of the disease, although constituting a general rule, is open to some exceptions. In the majority of cases only the legs and forearms are affected, and that in a symmetrical way; the other muscles may be involved more or less capriciously.

The weakness at first, and afterwards the paresis of the extensor muscles of the leg and of the flexors of the foot, and the trouble of sensibility, determining from the outset an imperfect perception of the ground, impart to the *gait* of the beriberic a characteristic feature. The first modifications in the gait may be observed as early as the end of the initial phase; they become, however, more accentuated as the disease progresses. At first the patients increase the distance between their feet in order to widen the base of support; at the same time they are very cautious, fixing their eyes on their feet and on the ground, fearing a fall or that their legs will not obey exactly the influence of the will. The gait may then be compared to that of a feeble person wading through a sheet of water reaching to his knees. Later on the gait becomes still more irregular; the patient raises his heels very high, walks on the outer edges of his feet, the toes dragging on the ground, and keeps the inner edges lifted high so that they do not touch the ground; hence often result irregular movements of the ankles, twisting of the foot, falls, and sprains. If the patient insists on continuing to go about, he drags his toes more and more in a way that reminds one of the pawing of a horse, and there is a greater flexion of the thigh exerted on the pelvis. After a few

steps the patient feels fatigued, seeks for support, and can no longer walk, unless when aided by another person, or using a cane to help himself along.

The patient has extraordinary difficulty in standing on one foot with his eyes shut, and even sometimes with them open; this difficulty, which may be observed from the outset of the disease, becomes more and more pronounced during its course. Romberg's symptom often exists. The sign of "defective marching in obedience to orders" may also be observed in beriberi in a not very advanced stage of its evolution; the patient has difficulty in rising suddenly, in stopping firmly and short in obedience to the order *halt*, and in turning round rapidly and without hesitation.

Sensory disturbances are constantly observed in beriberi. Among the first symptoms there is always a numbness of the skin, which delevops symmetrically, beginning in the legs and extending to the feet, and afterwards to the thighs. Frequently the numbness that the patient complains of in his feet and legs passes without transition to the hands, fingers, and tips of the fingers; the patient has difficulty in taking hold of surrounding objects and in buttoning his clothes. In some cases there is a certain regularity in the distribution of the anæsthesia; beginning in the legs, it descends, spreading over the instep, and ascends along the inner surface of the thighs; then the soles of the feet and the outer surfaces of the thighs are attacked. At the same time, or a little while after, it appears on the inner surfaces of the wrists, spreading over the backs of the hands, along the fingers to the finger tips and palms of the hands; it afterwards spreads to the forearm, elbow, and shoulder. The skin of the chest and abdomen is more rarely affected. According to Pekelharing the anæsthesia always spares the groin and neighboring regions. Simmons says that numbness around the mouth is frequent in beriberi; I have found this symptom in only two cases. The temperature sense to either heat or cold or both may be diminished or even suppressed in various parts, and there is often considerable loss of cutaneous sensitiveness to faradism. The diminution in the perception of heat and cold accompanies that of the sense of touch, and is localized in the same way. The sensibility to pain disappears more gradually; at first there is retardation in the transmission of painful impressions in regions where the numbness exists, and afterwards complete anæsthesia. In most cases the disorders of cutaneous sensibility are irregularly and capriciously distributed, there being alternate zones of more or less pronounced anæsthesia, hyperæsthesia, and paræsthesia.

The patient complains always of formication, tingling, pricking,

and other dysæsthesiæ; some say that the ground often seems elastic as if it were covered with thick layers of cotton, or unequal, or stuck full of needles which prick their feet; others, according to Costa Alvarenga, when they touch the roof of the mouth with the tongue, feel a sensation like that produced by hairs or threads. Hyperæsthesia is frequently observed, not only in the skin, but in the muscles, where it constitutes real myalgia, causing spontaneous or provoked pains; this hyperæsthesia is commonly observed in the calf muscles, and in those of the thighs and forearms. Tenderness of the nerve trunks may be observed, but far less in degree than in most forms of polyneuritis. The spontaneous pains sometimes assume the neuralgic character. Visceral crises, similar to those of tabes, have been seen; these are chiefly gastric, laryngeal, and urethral crises. When anæsthesia and hyperæsthesia coincide in the same patient, the singular phenomena of *anæsthesia dolorosa* may be observed.

At the beginning of beriberi, and even during the course of the disease, the patient often complains of a feeling of constriction, heaviness, and rigidity of the muscles, and painful cramps, especially in the calf muscles and those of the thighs. Overbeeck de Meyer and Pekelharing observed cramps involving almost all the muscles of the body, preceded and followed by fibrillary contractions.

A frequent symptom complained of by the patients, and to which Brazilian practitioners attach perhaps too much importance, is the feeling of tightness, strong pressure, or constriction like that of a belt over the epigastrium, spreading a little towards the hypochondria; when this feeling, which is called the beriberi belt, becomes intensified, the patient complains of breathlessness and a distressing feeling of oppression.

At the beginning of beriberi and often in what are denominated galloping cases, the cutaneous and tendinous reflexes are exaggerated; after some time, however, they become weakened, those of the lower extremities even disappearing in the advanced stages of the disease. Westphal's symptom exists almost always; indeed the knee-jerk is the one which becomes most weakened, and is the first to disappear in the advanced stages. I have seen cases in which it was absent in one knee, while it was only diminished in the other.

Disorders of the special senses of sight, hearing, taste, and smell seem to be more rare; nevertheless the medical literature of Brazil affords some observations of more or less pronounced ocular disorders, comprising strabismus, diplopia, amblyopia, and amaurosis, and also troubles of hearing, smell, and taste. I observed complete

loss of sight in two patients suffering from severe attacks of beriberi; both died two days after this symptom appeared.

Sensory disturbances as well as those of motion are often unstable; sometimes increasing, sometimes diminishing from one day to another, and sometimes remaining stationary during many consecutive days. It is common, for instance, to see a beriberic, who one day thinks himself unable to rise from his bed, feel able the next day to take a few steps and even to walk about a little.

The *œdema* forms a constituent part of the symptomatology of beriberi; it always commences under the skin over the edge of the tibia; it is hard and elastic, there being no pitting on pressure with the finger; the leg becomes round and acquires the shape of a pear whose smaller end would be represented by the not yet œdematous ankle. In many cases we observe only this œdema along the tibia, and a slight puffiness of the face. In some patients, as the disease progresses, the œdema gradually disappears, not to return; in most cases, however, it persists until the end, and may even spread to the ankles, feet, thighs, trunk, the root of the neck, arms, forearms, hands, etc. In some cases it amounts to actual anasarca, and spreads to the whole body, which becomes extraordinarily augmented in volume, and invades the lungs and serous cavities. It then loses the hard and elastic character observed over the tibia at the beginning of the disease, and resembles the œdema seen in the last stages of acute Bright's disease. In its progressive and ascending course the œdema does not always follow fixed rules; it may, for instance, pass from the legs to the upper extremities without affecting the thighs; it may be limited exclusively to the face, to the root of the neck, to the two upper extremities, to the hands, to the instep, to the sides, etc. Malcolmson observed a patient in whom the œdema existed only along the spine and in the lumbar and sacral regions. It often remains limited to the legs, ankles, and feet. Usually symmetrical, it may, however, develop only on one side, and may even be crossed, as was the case in a patient of Bourat, who presented infiltration in one side of the face and in the extremities of the opposite side. The œdema may present the greatest irregularities as to its manner of development and retrogradation; usually beginning in the legs, it spreads little by little upwards and downwards, and when the disease tends to a cure it gradually disappears. In some cases, however, it is seen to appear suddenly, attaining in a few days or even hours a frightful development; in others it remains limited to certain points during many weeks. It may disappear suddenly, its disappearance being followed by profuse diuresis; or it may disappear from one region to invade another symmetrical or neighboring one.

Œdematous infiltration of certain organs and effusions into the serous cavities sometimes coincide with the cutaneous infiltration. Œdema of the lungs is a serious accident, and may be the cause of death; its symptoms vary accordingly as the development is sudden or gradual; in the former case it commences bruskly by an extreme oppression, a violent dyspnœa, accompanied soon after by signs of asphyxia; very abundant seroalbuminous expectoration takes place at once; on auscultation a fine moist crepitation or subcrepitation is heard over the whole of both lungs; the resonance is exaggerated by reason of the acute emphysema that accompanies this œdema; the symptoms of asphyxia become more and more pronounced, and death may occur within a few hours. The gradual development of the pulmonary œdema is marked by a cough, slight at first, and afterwards fatiguing, by abundant, frothy, and fluid expectoration, sometimes of a pink color owing to the admixture of a small quantity of blood, and by dyspnœa which goes on increasing with the progress of the infiltration.

The effusion of fluid into the serous cavities is not so frequent as has been asserted. Up to the present, I have observed during the life of the patient hydropericardium only four times, and ascites once; in this latter case the effusion was not great. I have never seen hydrothorax; Torres Homem, however, speaks of a patient in whom there was a rapid development of an abundant dropsy of the left pleura accompanied by intense dyspnœa, which yielded after the withdrawal of the fluid.

The elastic œdema of the edge of the tibia, that which lies between the muscular bundles, and the puffiness of the face are due to the vasomotor neuritis; the flaccid subcutaneous dropsy, the pulmonary œdema, the anasarca, and the effusions of fluid into the serous cavities are owing to cardiac weakness. This last factor, however, though sometimes sufficient to explain the development of generalized œdema, is not so at other times, and in such case paralysis of the vasomotor nerves must be admitted, for this may of itself suffice to cause the generalized œdema.

The *muscles* in beriberi exhibit a constantly altered condition; they are sometimes atrophied and sometimes enlarged; and both atrophied and swollen muscles are sometimes found in the same patient. The muscular atrophy may be found in some muscles only or in groups of muscles, and may also invade all the striated muscles of the whole body. In relation to its intensity, the atrophy assumes various degrees; for instance, in dry beriberi the legs, in the last period of the disease, appear to consist entirely of skin and bones. In the hands the thenar and hypothenar regions are depressed, the interossei and lumbricoid muscles become thinner.

The atrophy may be in some cases disguised by the infiltration of fluid between the muscular bundles. The apparent muscular hypertrophy that is often observed, and which, when it assumes a great intensity, constitutes what is called the *polysarcous beriberi* of Oudenhoven, is due to the swelling of the muscles, and may also depend in some cases, as is shown by the autopsy, on an exaggerated development of the muscle fibres, attended with degeneration. The swollen muscles feel hard and firm to the touch, and when contracting may present circumscribed areas of enlargement. According to Anderson, indurations in the calf muscles, symmetrical and apparently confined to the inner belly, are often met with in chronic cases. Both the atrophied and hypertrophied muscles may be very painful on pressure. In subacute cases, there is often an increase of mechanical irritability, which coincides almost always with the increase of galvanic irritability. When examined electrically the affected muscles and nerves exhibit a more or less pronounced diminution of the irritability for both the galvanic and faradic currents, and a partial or complete reaction of degeneration. At the beginning of the disease, or coinciding with the acute exacerbations, there may be a very short period of increase of irritability in some muscles and nerves.

Temperature.—For many years beriberi was considered an essentially apyretic disease, and writers asserted that the fever sometimes observed was independent of the disease, and due to a cause foreign to it. All observers are to-day agreed that in the advanced stages there is no fever, and that the temperature may be subnormal; this last symptom always indicates a serious condition and the approach of death. The same unanimity, however, does not exist in relation to the possibility of fever at the outset or during the first stages of the disease. Very recently A. Bentley wrote that "the temperature charts are of interest from their negative results. In no case could an onset of acute symptoms have been foretold by the observations of the temperature chart. It is essentially a non-febrile disease." To Professor Saraiva, of Bahia, belongs the merit of having called attention very positively to the existence of beriberic fever, and he has described with accuracy the acute febrile forms of the disease observed by him during the Paraguayan war. Later observations have shown the possibility of a febrile temperature independently of complications during the course of beriberi. According to Schutte the temperature varies considerably; sometimes we observe cases free from fever; others exhibiting a frank febrile condition, chiefly in acute forms of the disease; then the fever is continued, attended with thirst, exaggerated palpitations, dyspnœa, and prostration; some-

times the febrile temperature and apyrexia alternate. From what I have observed myself I conclude that the fever in beriberi is inconstant and very irregular as to appearance, duration, and type. In some patients the disease runs its course from beginning to end without fever; in others there is fever whenever acute exacerbations of the symptoms occur during the first stages. The fever may or may not be preceded by chills; it may last one or more days, the temperature rising to about 39.5° C. (103.1° F.); and the febrile type may be continuous, remittent, or intermittent. In most cases the fever occurs during or just after the initial stage of beriberi. Patients state that the numbness and other symptoms appeared after an attack of fever, or that a few days after the appearance of those symptoms they had fever. When it occurs during the initial phase, the fever is often supposed to be due to a cold or to a gastric indisposition, and when beriberi is confirmed and the patient demands medical attention, he often forgets to refer to that fever. P. Manson, in Hong-Kong, had the opportunity of watching, in a small number of attacks, the development of beriberi from its commencement. The patients had been admitted to the hospital for various non-febrile surgical diseases. As a matter of routine the temperature was regularly taken night and morning for some time before beriberi declared itself. They were quite free from fever on admission, and for a considerable period thereafter showed no signs of beriberi. Seven of the hospital patients were affected by this disease, and in each of them, soon after the appearance of the premonitory numbness, there occurred more or less marked, sometimes severe, pyrexia, preceded by rigors.

The *blood* is not always found to be altered in beriberi. Wernich observed that the blood corpuscles are not arranged in rouleaux as in health; that they exhibit a great number of crenated forms, and that certain brilliant groups are found in the blood; besides these disorders, he always observed a constant hypoglobulia. Accurate observations made afterwards in Brazil, Japan, and Java, especially by Martins Costa, Magalhães, W. Taylor, and Eykman, showed that beriberi has nothing whatever to do with anæmia. The latter may be observed, however, in the advanced stages of the disease, as a consequence of it or owing to a complication—malaria, ankylostomiasis, etc. As a rule, we may say that in beriberi, especially in the first stages, there is no diminution in the number of red corpuscles or excess of the white ones. The red corpuscles arrange themselves in rouleaux; there is no excess of crenated corpuscles, microcytes, or granules.

The *pulse* in beriberi is subject to great variations in different

patients and in the same patient at different times, but these variations are always in harmony with the cardiac disturbances. In some rare cases, at the outset, the pulse may be full, strong, and slow; the number of beats is then below the normal; this fact coincides with an increase of the contractile energy of the myocardium and a more pronounced impulse of the heart apex. In most cases, however, the examination of the pulse shows that the dynamic condition of the circulation is one of relaxed arterial and vasomotor tension, with diminished cardiac power. Wernich demonstrated with numerous sphygmographic tracings that during the whole course of the disease the tension in the arterial system remains low, but rises in convalescence. Taylor describes the pulse-tracing in beriberi as being characterized by: (*a*) very sudden and high upstroke; (*b*) precipitous descent from the apex of the percussion wave; (*c*) dicrotism. The sudden and high upstroke indicates cardiac excitement, the precipitous descent diminished vasomotor tone. In some cases the pulse may be very weak, irregular, and frequent, sometimes reaching 150 per minute; there is true tachycardia; the præcordial impulse becomes considerably weakened and the sphygmograph, or better still the sphygmomanometer, reveals a great reduction of arterial tension. In almost all patients intermittences of the pulse are observed; they are exceedingly irregular; for instance, when the pulse is counted several times, the number of pulsations is never found to be the same; there is always irregularity in the intermittence. We may count two or three beats, followed by a pause, immediately afterwards five or six beats and another pause, and then four, five, or eight beats consecutively and so on continually varying.

Heart.—Almost all patients complain of palpitations of the heart from the very earliest stages of the disease. At first palpitations occur in consequence of some effort or exercise, but later they appear spontaneously, in more or less lasting and troublesome paroxysms. In some patients they are attended with a feeling of præcordial oppression, which may turn into an attack of angina pectoris, with a piercing and constricting retrosternal pain spreading to the shoulder and left arm, with dyspnœa, etc. Although Francisco de Castro states that he has observed true and complete attacks of angina pectoris, I believe them to be exceedingly rare; I have, however, observed mitigated and incomplete forms.

The direct examination of the heart always reveals more or less pronounced alterations, which are perceived from the initial stage of beriberi. By palpation one can recognize an increase of the diffuse cardiac impulse; in the last stages of the disease the impulse is often found to be diminished. By percussion one can observe an

increase of the precordial dulness, which extends beyond the right border of the sternum, revealing an increase in volume of the right heart; sometimes there is also an increase in the area of cardiac percussion dulness towards the left side.

Observers (chiefly Brazilians, who, better than any others, have described the cardiac symptoms of beriberi) are not agreed concerning the disorders revealed by auscultation of the precordial region. They mention systolic or diastolic murmurs heard over the different valve areas of the heart, reduplication of the first or second sound, with a maximum of audibility, now at the apex, now at the base, triple murmurs, and galloping rhythm. From the reading of the works published on the subject, it must be concluded that beriberi is attended with constant cardiac troubles, among which are to be noted modifications of the rhythm of the heart and quantitative and qualitative alterations of the sounds. One point upon which all practitioners seem agreed is the accentuation of the pulmonary second sound, observed for the first time by Francisco de Castro, of Rio de Janeiro. Seldom is a case of beriberi seen without the presence of this cardiac sign from the very outset of the disease, and this constitutes a good element of differential diagnosis between beriberi and the other forms of polyneuritis.

The other physical signs revealed by auscultation of the precordial region vary exceedingly in the same and in different patients. In many cases, during the entire evolution of the disease, the accentuation of the second pulmonary sound is the only alteration heard. In some patients murmurs, usually of mesosystolic or systolic character, coming and going, are heard over the different valve areas of the heart, almost all, however, having their maximum of audibility in the third intercostal space a few centimetres above the point of the apex beat. They are almost all soft, superficial, with restricted area of propagation, disappearing when the patient is in an erect posture, which shows them to be extracardiac. In the more advanced stages of the disease there is often heard in some patients a soft and blowing systolic murmur, with maximum differential intensity at the lower end of the sternum or adjacent costal cartilages, and with direction of propagation upwards and to the right. This murmur indicates a relative tricuspid incompetence, consecutive to the dilatation of the right cavities of the heart. The reduplication of the second cardiac sound is in my opinion more frequently observed in beriberi than are the murmurs. This reduplication is better perceived at the base of the heart, at the end of inspiration and beginning of expiration, and always coincides with the accentuation of the pulmonary second sound. Dr. Almeida Magalhães, who studied it carefully, asserts

that there is always precedence of the aortic sound. I think this assertion rather absolute, and I believe that we can observe sometimes precedence of the aortic sound, sometimes that of the pulmonary sound, according to the conditions. As to the reduplication of the first sound, met with in beriberi by Torres Homem, Silva Lima, and F. de Castro, I think it very rare; at least I have never had the opportunity to observe it. Like the murmurs, the reduplications are very unstable, appearing and disappearing in the same patient, sometimes lasting hours and sometimes as long as several weeks. Some Brazilian writers consider the galloping rhythm as one of the cardiac symptoms of beriberi; from their description, however, it is to be inferred that they often confounded the galloping rhythm with the reduplication of the first or second sound. I have never observed the presystolic galloping rhythm, with maximum audibility in the regions of the middle part of the left ventricle or in the region of the apex, which forms a part of the symptomatology of the interstitial form of Bright's disease. Indeed, I believe that when it exists, it always indicates some complication or the presence of a concurrent disease, because beriberi does not possess the conditions necessary to its development, that is, increase of tension in the great circulation and diminution of tonicity in the left ventricle. The prediastolic gallop or right gallop, however, with maximum audibility at the lower end of the sternum, may be found in the course of beriberi in some cases, as was remarked for the first time by Almeida Magalhães.

Cardiac troubles in beriberi are not easy of explanation, and their mechanism cannot be said to be perfectly established. Some writers consider them all subordinated to neuritis of the vagus; Nina Rodrigues, without denying the influence of alterations of the vagus, believes that the lesion of the sympathetic is the principal factor in the cardiopathies of beriberi. Dr. Almeida Magalhães has recently proposed a somewhat ingenious explanation; he considers the increase of the tension in the pulmonary circulation as the starting-point of the cardiac troubles, this increase being revealed by the accentuation of the second pulmonary sound, by the reduplication of the second sound, and by dilatation of the right cavities of the heart. He believes that the poison irritates the thoracic ganglia and the nerves which, branching off from them, are distributed to the vessels of the lungs; the irritation is attended with vasoconstriction, and consequently, with increase of tension. This irritation theory seems acceptable only in the first stages of beriberi; in the more advanced stages, or during acute exacerbations attended with grave disturbances of the circulation, it is not sufficient to explain the symptoms and lesions observed. On the other hand, the irritation of the tho-

racic ganglia is not sufficient to explain all the disorders of the cardiac rhythm, the irregularities and intermittencies of the pulse, for instance. Besides this, the irritation of the ganglia and nerves being protracted, it is to be supposed capable of causing the inflammation and ulterior destruction of them, and then vasodilatation would take the place in the lungs of the primary vasoconstriction. The pathological physiology of the cardiac troubles in beriberi is more complex than it seems; it should be sought in the alterations of the sympathetic, the automotor ganglia, and the pneumogastric. When myocarditis exists, either due to the direct action of the beriberic poison on the cardiac muscles or consecutive to alterations of the nerves, it explains some of the troubles, among them the right galloping rhythm.

Digestive Organs.—In a great number of cases of beriberi the appetite holds out, and the digestive functions are fairly well performed. There may be observed, however, from the beginning of the disease a loss of appetite, a furred tongue with loss of its epithelium, nausea, vomiting, and diarrhœa or constipation, these two symptoms being liable to alternate in the same patients.

The liver and spleen remain normal during the greater part of the evolution of the disease, and when they are affected the explanation is to be found in a complication foreign to the beriberi. In the more advanced stages, however, the liver is often found increased in volume and slightly painful on pressure.

Genitourinary Organs.—In some patients there is a diminution of sensibility of the mucous membrane of the bladder; there is a desire to urinate only when the bladder is very full; others find some difficulty in urinating, owing to a slight paresis of the bladder, or to weakness of the abdominal muscles; others complain of a burning sensation and even sharp cutting pains along the entire course of the urethra, during the passage of the urine. In the majority of cases, however, this function is not affected.

The urinary secretion is often diminished; in some patients in the œdematous forms of beriberi, it may be reduced to 300 or 200 gm. a day, and may even be completely suppressed, constituting true anuria. Whenever this happens, the patient exhibits symptoms of uræmia, which will be the more intense and rapid the greater the decrease of uropoiesis. Francisco de Castro was the first writer to call attention to beriberic uræmia coming on without preceding albuminuria. The diminution of the urinary secretion and anuria in beriberi may be due to a great venous congestion of the kidneys determining a compression of the urinary ducts and the afferent arteries; this venous congestion is in its turn caused by the low

arterial tension. But the arterial tension is not always so low as to be able to provoke a venous congestion of the kidneys sufficient to produce anuria. Nina Rodrigues believes that beriberic anuria is due to an œdema of vasomotor origin of the cortical portion of the kidneys, and since the tissues at this point are inextensible, the œdema exercises compression on the afferent vessels, determining an exudation in the ducts. This explanation, which was proposed by Rénaut, of Lyons, to account for the false renal impermeabilities of interstitial nephritis, seems to me worthy of acceptance in relation to beriberic anuria. The polyuric crises that often succeed the complete suppression of the urine, the elimination during them of great quantities of urea, and the constant implication of the sympathetic nerve in mixed and dropsical forms of beriberi, are an indication in favor of renal œdema.

The urine in beriberi is usually acid, its density varying according to the greater or less amount secreted; it deposits sediment, is slightly colored, and contains almost always a smaller percentage of urea. Albumin is absent in the great majority of cases; when found in the urine, its presence should be attributed to an accidental complication, or to an intercurrent disease, or to a blood stasis in the last period in grave cases. Not infrequently the disappearance of the œdema coincides with an abundant diuresis.

The beriberic patient frequently loses all sexual desire, and during the whole evolution of the disease there is a sensible decrease of sexual potency, sometimes reaching a state of complete impotence. Women complain of menstrual troubles, the flow being sometimes less abundant, sometimes delayed, and sometimes even suppressed.

Lungs.—Besides the symptoms indicative of pulmonary œdema, the examination of the lungs may reveal the existence of others, which denote respiratory trouble independently of serous infiltration. After the slightest exercise the breathing becomes irregular, hurried, panting; sometimes, soon after the initial phenomena, there is dyspnœa, which becomes rapidly worse; the breathing in a short while becomes diaphragmatic, afterwards the diaphragm is affected in its turn, and the patient dies suffocated. At other times the dyspnœa comes on in attacks coinciding with cardiovascular troubles, accompanying the paroxysms of angina pectoris, or when the feeling of constriction known as the beriberic belt becomes aggravated. Finally, in many cases, the patient is taken during the night, or even in the day, with violent fits of suffocation, similar to asthmatic dyspnœa, which yield rapidly to hypodermic injections of morphine.

Skin.—The secretion of sweat diminishes considerably and totally disappears in some cases, the skin being dry, rough, and corky. In

a few cases an abundant secretion of sweat has been observed, either general or limited to a certain region. Some patients suffer from cutaneous eruptions of various forms, similar to those of roseola or erythema. In very rare cases may be observed certain trophic disorders such as shedding of the hair, alterations of the nails, etc.

Classification.

As may be inferred from the above description, the symptoms of beriberi are very numerous, varying a great deal as to greater or less frequency in patients. Even the most constant symptoms, such as depend on paresis, atrophy, numbness, and œdema, may be present in very variable combinations; and by way of facilitating the diagnosis it is usual for authors to study them from the point of view of their grouping and succession, classifying the cases according to the relative predominance of certain symptoms, and describing special clinical forms.

Former observers described two clinical forms, namely, the œdematous, or wet, and the atrophic, or dry; while some, finding great differences between the two forms, considered them as distinct nosological entities. Such classifications, however, did not correspond to the exigencies of the diagnosis, being rather a cause of embarrassment, because the paralysis, atrophy, and œdema are often associated in varied proportion, it being exceptional to meet with a case of dry beriberi without œdema, or one of wet beriberi without sensory, motor, and amyotrophic disorders. To the Brazilian physician Silva Lima belongs the merit of having facilitated the diagnosis of beriberi by describing with great precision the mixed form, which is the most frequent. After the works of Silva Lima, the clinical division of beriberi into three forms has become classical. These three forms are the paralytic, the œdematous, and the mixed.

Recently some authors have admitted new clinical varieties. Oudenhoven described a polysarcous form; Oveerbeck de Meyer a convulsive form; Scheube considers the symptoms of beriberi susceptible of grouping in four different ways, constituting four clinical forms: (1) the mild form; (2) the atrophic form; (3) the dropsical or hydroatrophic form; (4) the acute pernicious form. Corre is still more confused in describing the hyperacute, acute, subacute, chronic and abnormal forms, either simple, associated, or complicated. Wernich, in addition to a galloping kakké terminated by death within a few hours or days, recognizes subacute and chronic forms. After the investigations of Pekelharing and Winkler, confirmed in Brazil and Japan by many other observers, it is no longer permissible to admit

without discussion the so-called hyperacute and acute forms. Indeed, the Dutch savants have shown most clearly that beriberi is a chronic disease, developing at first slowly and exhibiting at a later period of its evolution acute aggravations. Under these circumstances, the greater or less rapidity of development may constitute at most a clinical variety and not a special form, since in all stages of the disease may be observed the hyperacute or acute aggravation, now limited to a group of symptoms, now general throughout the symptomatology. As regards the convulsive beriberi of Overbeeck de Meyer I consider it a mere variety, since the symptoms that characterize it are observed during a limited stage of the evolution of the disease, lasting generally a short time, and do not therefore combine the indispensable requisites in nosology to constitute a special clinical form. I may say the same in relation to the polysarcous beriberi of Oudenhoven and the so-called gastric, cardiac, pulmonary, uræmic, and other forms of other authors.

The classification of Silva Lima deserves to be retained, as being that which best corresponds to the necessities of the diagnosis; and that which, with the greatest fidelity and simplicity, embraces the numerous clinical features of the disease.

The beginning of beriberi, whatever be the clinical form it afterwards assumes, is always represented by the symptoms I have described as forming part of the initial stage. This stage, the duration of which is very variable, being over, the prevalence either of sensorimotor and atrophic symptoms, or of œdemas and serous effusions, with grave disturbance of the circulation, or the assemblage in one patient of all these disorders in more or less equal parts, will characterize the three clinical forms of the disease: paralytic or atrophic, dropsical, and mixed. Each one of these forms admits of several divisions, according to the predominance of one or another group of symptoms; one may describe the convulsive, polysarcous, visceral, uræmic, acute pernicious varieties, etc.

The *mixed form* is the most frequent of the three; after an initial stage of somewhat long duration, there is a gradual increase of numbness and of motor paresis, coinciding with spontaneous or provoked pains of the calf mucles, and itching in the feet, hands, and fingers; in a short while the tendinous reflexes are found considerably diminished or even suppressed, and the cutaneous reflexes normal or diminished; then comes difficulty in walking and standing; the patient complains of the belt feeling; the œdema spreads to the ankles, to the instep, to the legs, thighs, and face, and sometimes to the upper extremities; the serous infiltration takes place not only under the skin, but between the muscles, which gives to the legs and

thighs a rounded shape; frequent and troublesome palpitations occur spontaneously, or in consequence of the slightest effort; the pulse is unequal and intermittent; examination of the heart reveals the existence of dilatation with hypertrophy of the right ventricle, increased area of the impulse, accentuation of the pulmonary second sound, and sometimes reduplication of the second sound, with maximum audibility at the base of the heart; the patient complains of fatigue and shortness of breath. This type of beriberi is the one most commonly observed in Brazil; the symptoms described remain sometimes stationary for a long time; often, however, they present examples of great instability, now increasing gradually or suddenly, now abating in a more or less pronounced manner, then growing worse again, and so on. Acute aggravations are very frequent in the mixed form, and are sometimes attended with fever of a subcontinuous or remittent type, or with gastric disorders, or with fits of dyspnœa or serious circulatory disturbances, attended or not with paroxysms of angina pectoris. Sudden death often occurs during one of these acute aggravations, owing to cardiac paralysis or to asphyxia, resulting from the progress of the pulmonary œdema or from paresis of the respiratory muscles.

I had occasion to observe in 1889, in Rio de Janeiro, a case in which I had at first made a diagnosis of general infectious polyneuritis, but which I later recognized as beriberi. The patient was carried to the hospital, presenting very pronounced sensory and motor disorders in the upper and lower extremities, being unable to remain standing or even sitting, having pains in the calves, suppression of the tendinous reflexes, and great diminution of the cutaneous reflexes; slight puffiness of the face and skin; the right heart was increased in volume; there was accentuation of the pulmonary second sound; permanent dyspnœa due to paresis of the intercostal muscles; a hoarse and weak voice. Death occurred on the second or third day after his entry in the hospital, and was due to the progress of the asphyxia, the diaphragm being paralyzed.

The *œdematous or dropsical form* is incontestably the rarest of the three; it is characterized by the prevalence of œdemas and serous effusions over the paralytic disorders. After an initial stage of long duration, the cardiac symptoms become more and more pronounced, and the œdema, at first limited to the legs, extends downwards and upwards, acquiring in a short time a great development and assuming the proportions of true anasarca. In its invading course the serous infiltration always reaches the lungs, and may invade the pericardiac, peritoneal, and pleural cavities. Symptoms of cardiac and renal weakness prevail, the sensorimotor disorders being relatively

trifling. Then are observed dilatation of the right cavities of the heart, attended with the usual symptoms of cardiac asystolia; crises of dyspnœa, connected with pulmonary œdema, or deficient renal secretion; more and more accentuated diminution of the quantity of urine voided, sometimes going so far as to constitute anuria. The symptoms that characterize the œdematous form may develop on occasion of an acute exacerbation in a mixed beriberi of more or less long standing. They often yield to treatment, and the disease continues its course after the distressing symptoms of cardiac and renal insufficiency have disappeared. When death occurs, it is the result of the œdema of the lungs, hydropericardium, or uræmic intoxication; sudden death may result from syncope caused by sudden paresis and collapse of the weakened heart.

The œdema is not entirely absent in the *paralytic form;* a slight puffiness of the face and a trifling œdema along the edge of the tibia are observed from the outset and persist for some time after the initial phase; they sometimes become worse, but afterwards disappear as the disease progresses. What characterizes this form, however, is the great prevalence of sensorimotor and atrophic disorders. The motor paralysis initiated in the lower extremities progresses, becoming worse and worse; in a short while the patient encounters the greatest difficulty in walking, and his gait becomes characteristic; the affected muscles become thin and the atrophy, limited at first to some muscle or group of muscles, tends to become general. The electrical examination reveals the existence of a reaction of complete degeneration. The atrophy may be preceded by phenomena of irritation in the muscles, fibrillary contractions, and more or less extensive and intensive cramps, which sometimes give to the disease a peculiar feature. During the evolution of the paralytic form acute or hyperacute exacerbations may be observed, often terminated by death, which occurs within a few hours or days. In the last stages of the disease the patient is confined to his bed, being unable to make a step, and in a state of extraordinary emaciation. Notwithstanding the paralysis and the great atrophy, the functions of organic life are usually well executed; the appetite may remain good or be slightly diminished; the bowels act regularly; the urine, normal in quantity, does not contain albumin, but is voided with some difficulty, owing to paresis of the abdominal muscles; the senses of sight, hearing, smell, and taste are usually spared; and the cerebration would be perfectly good but for the more or less pronounced impairment of memory.

If death does not occur, months elapse before the atrophied muscles regain their physiological integrity, and many of them

remain useless forever. The cause of death is in most cases suffocation more or less rapidly developed, owing to the paralysis of the diaphragm and of the intercostal muscles, or to a lesion of the vagus and its ramifications, or even to pulmonary œdema.

Anderson gives a good description of the symptoms that often precede death, occurring during one of the acute or hyperacute paroxysms in beriberi. He writes: "The grave symptoms may appear without warning, nearly always developing in the course of a subacute or chronic attack. A patient comes under treatment for kakké of apparently an ordinary character; he is usually strong and well nourished, has no sign of anæmia, and little or no œdema; the disease progresses in the usual manner, and no evil is anticipated, when suddenly rapid action of the heart, strong pulsation in the neck, and difficulty of breathing appear, with a distressing pain in the abdomen. Soon afterwards the patient vomits; and while an observer unaccustomed to see the disease still apprehends no danger, the Japanese doctor recognizes the commencement of 'shiyoshin' and predicts that the man will surely die. During the next few hours the breathing becomes more embarrassed, the pulsations of the heart more and more accelerated, and vomiting occurs from time to time. The patient can lie down no longer; he sits up in bed or tosses restlessly from one position to another, and with wrinkled brow, staring, anxious eyes, dusky skin, blue parted lips, dilated nostrils, throbbing neck, and laboring chest, presents a picture of the most terrible distress that the worst of diseases can inflict. There is no intermission even for a moment, and unless active treatment be at once resorted to the pulse fails, the temperature sinks, and at length the brain, paralyzed by the carbonized blood, becomes insensible, leaving the dying man to pass his last moments in merciful unconsciousness."

Duration.

A disease with a chronic course, subject to acute paroxysms, many of which are terminated by death, being sometimes rapidly cured when the patient changes his residence, at other times remaining stationary for a long period, or growing worse very slowly when the patient remains in the endemic centre, beriberi has a variable duration, which may be computed between five weeks and two years. Cases of over two years' duration have been mentioned; I believe that in these cases, as well as in many of those which have a duration between one and two years, there are real relapses of the disease. Relapses are very frequent in beriberi; sometimes three, four, or five occurring in the same pa-

tient; there are persons who exhibit symptoms of the disease every time they return to the endemic centre, and are compelled to leave again at once.

Pathological Anatomy.

The beriberic cadaver presents various aspects according to the predominant clinical forms and to the alterations that were the cause of death. When, during life, the paralytic and atrophic form predominated, the body may appear as lean as in progressive muscular atrophy. These cases are not very numerous, however, muscular atrophy and pseudohypertrophy often being associated, accompanied with slight œdema of the lower limbs and swelling of the face. When, during life, the dropsical form predominated, the body presents an aspect similar to that which is observed in individuals having died from Bright's disease; if an incision is made in the skin, the presence of serous fluid in greater or less abundance may be recognized in the subcutaneous cellular tissue, and in and between the muscles. If death was violent, owing, for instance, to the sudden arrest of the heart's action, or to paralysis of the respiratory muscles, the painful agony remains stamped on the feature. The face is swollen, cyanosed, the eyes appear ready to start from their sockets, ecchymoses are seen in the conjunctivæ, the jugular veins resemble thick blue cords under the skin, the mouth remains half open, and the lips are covered with frothy saliva.

The post-mortem examination often reveals the presence of effusions in the serous cavities. Dropsy of the pericardium is constant; Pekelharing in 64 autopsies found little or no serosity, twice; from 20 to 50 gm., 20 times; from 50 to 100 gm., 13 times; from 100 to 250 gm., 17 times; and more than 250 gm., 12 times. In the same number of autopsies he found hydrothorax 14 times and ascites 9 times. Œdema of the lungs is also frequent; Pekelharing observed it 23 times.

Alterations of the *heart* are constant in beriberi: there is always hypertrophy of the right ventricle, attended with dilatation, which may assume a fearful character. The left heart is also found hypertrophied and dilated, but to a less degree. Scheube in his examinations found the dilatation of the right cavities of the heart 70 times in 100; dilatation of both cavities, 20 times in 100; hypertrophy of the left ventricle, 25 times in 100; hypertrophy of both ventricles, 20 times in 100. Baelz always found the heart increased in volume, the left ventricle thickened and the right one dilated. Pekelharing never found a beriberic heart weighing less than 250 gm.; in his 64

autopsies the heart weighed from 250 to 300 gm. in 5 cases; from 300 to 350 gm. in 42 cases; from 350 to 450 gm. in 17 cases. In the few autopsies I have performed I have always found a great increase in the volume of the heart, hypertrophy and dilatation of the right ventricle predominating. Scheube describes a fatty degeneration of the heart of a distinctive character, and thinks it is always secondary to a neuritis of the vagus. The degeneration is diffused over the heart muscle, and affects the right ventricle more than the left. P. Pereira and Lacerda always found this fatty degeneration. Miura says it is not constant. Pekelharing asserts that fatty alteration of the heart is seldom observed, and that, when it does exist, it is very slight. Baelz says he never met with it, and that the microscope always reveals a very clear striation of the muscular fibres. He found in the heart of beriberics points of interstitial myositis, with dilatation of the lymphatic spaces by fibrinous coagula. Scheube in two cases found, in the cardiac muscle, especially in the right ventricle, inflammatory alterations, partly in small disseminate foci, partly in diffuse interstitial infiltration, resembling diphtheritic interstitial myocarditis. Lacerda describes more or less extensive foci of degeneration and circumscribed inflammatory areas, the last appearing in the layers nearest to the apex, and consisting of an accumulation of nuclei and migrating cells.

The *liver* and *spleen* appear sometimes normal, at others congested or altered by fatty degeneration. Pacifico Pereira always found them fatty. The *lungs* are generally gorged with blood, and may be œdematous.

According to Baelz the *kidneys* are nearly normal as regards appearance and size; the epithelium of the tubuli contorti is sometimes a little swollen; the outline of their cells is not easily distinguishable, and their nuclei are difficult to see. After death, as during life, no signs of true nephritis are to be found. According to Scheube the kidneys are generally full of blood. The cells show some cloudiness of nuclei and fatty deposit in the protoplasm, often visible to the naked eye. Small hemorrhages in the pelvis were seen twice. In some hardened sections a few groups of cells are found, as a rule immediately under the capsule. According to Miura the epithelium of the kidneys is often swollen, degenerated, and finely granular. The tubules are filled with homogeneous cylinders or fine detritus; the stroma is filled with small cells; there is occasionally distinct increase of the connective tissue, with injection of the small vessels, whose walls are thickened. The glomeruli are filled with nuclei, of normal size, or enlarged, or diminished in size as a result of exuda-

tion between the capsule and glomeruli, evidently a condition of glomerulonephritis (Bentley).

Lesions of the *muscles* are frequent, being seen chiefly in the paralytic form of beriberi; atrophy is always found and often hypertrophy, or rather swelling, coinciding with the former. In much atrophied muscles a dark yellow color prevails; in swollen muscles yellow streaks and flesh-colored spots alternate, giving them an appearance of marble. In most cases, according to Scheube, there are atrophy and fatty degeneration of the muscular fibres, with increase of nuclei. At the same time, there is frequently a degeneration similar to colloid by reason of which the muscular fibres become thinner and homogeneous, and are reduced to fibrils; true colloid metamorphosis is seldom observed; in place of the muscular fibres that are atrophied and that disappear completely or in part, connective tissue and newly formed nuclei are found, and remarkable inflammatory alterations of the vessels manifest themselves. According to Pekelharing the microscope reveals the presence of finely granular muscular fibres, others with the appearance of wax, with indented border, other swollen and rounded, others simply atrophied, and, finally, some in which the atrophy is accompanied with an increase of nuclei, the transverse striation, however, being preserved.

Nervous System.—Before Baelz had clearly described the specific alterations of the peripheral nerves in beriberi, observers had busied themselves a great deal with the lesions of the nervous system, chiefly of the spinal cord. These lesions, however, were always found to be so various and inconstant that they could never be considered as peculiar to beriberi. There were found in persons who had died of this disease, more or less pronounced congestion or œdema of the meninges of the brain and of the medulla; partial or total softening of the spinal cord; alterations of the anterior and posterior roots of the spinal nerves; alterations of the cells of the anterior cornua; amylaceous corpuscles in the spinal cord, cerebrum, cerebellum, bulb, etc. Pekelharing, in ten autopsies, found the medulla perfectly normal six times; with probable but trifling modifications in the two radicular zones, three times; with distinct alterations in the posterior cord, once. Scheube in one single case found atrophy and partial disappearance of the ganglion cells of the anterior cornua. Miura in three cases found vacuolation of the cells in the anterior horn. The vacuoles occur singly or in groups of various sizes, sharply differentiated from one another, and always in the neighborhood of the nucleus; the body of the cells is often largely occupied with the vacuoles, while the nucleus is little altered. Bentley found the spinal cord in all the cases enormously congested—softened and

œdematous in some; the brain was also found by him congested as well as the dura mater.

Baelz was the first to describe the alterations of the *peripheral nerves* in beriberi, and to show that they are constant. His description was confirmed and completed by Scheube, Pekelharing and Winkler, and others. On examination, the peripheral nerves, besides some normal or almost normal fibres, present many degenerated ones, showing various alterations according to the degree of the pathological process. Now the nerve fibre appears thicker, the myelin sheath loses its regular form of a double outline cylinder, and appears segmented; the medullary substance is wanting at the level of Ranvier's nodes, where may still be seen the axis cylinder; again the myelin presents itself broken up, all changed into granulations; at the level of the interannular nuclei are found two or three colored nuclei; the myelin then disappears entirely, and with it the axis cylinder, leaving the nerve tube reduced to the empty sheath of Schwann. The nerve fibres may, moreover, appear thin with swellings at certain places; in the swollen places are found small black or yellow colored globules, perfectly mixed with a frothy mass, which takes a light pink hue by the addition of carmine; by reason of the absence of the myelin, the sheath of Schwann collapses; on the inside may be seen several very fine fibrils; a colorless cone limits the frothy mass, and at its level may be observed the fibrillary structure of the contents of the nerve tube. In many cases there is an increase in the number of the nuclei of the endoneurium, and pronounced inflammatory alterations of the blood-vessels. The known lesions of the periaxial segmental neuritis of Gombault are sometimes found in the nerves. In chronic cases there is hyperplasia of the endoneurium of a gelatinous nature. The increased connective tissue crosses in the interior of the nerve bundles, forming thick septa which frequently divide a few nerve fibres into a great number of distinct parts.

The lesions of beriberi are irregularly disseminated; in the same nerve trunk certain of the tubes are found almost normal, if not entirely so, and others the myelin of which is broken up in large pieces; fine fibres, empty Schwann's sheaths, fibres presenting alterations of periaxial neuritis, and finally proliferation of the interfascicular connective tissue; dilatation of the vessels, extravasation of blood, etc., are also met with. The lesions are not uniformly distributed throughout all the nerves; even in the same nerve they are more accentuated at the periphery, and go on diminishing towards the centre. The spinal roots, both anterior and posterior, are in most cases found in a normal condition.

From the above description it is to be inferred that the more constant and perhaps more important lesions in beriberi are found in the peripheral nerves; but besides these there are others, which cannot occupy a secondary place. Indeed, if some of them must be considered as direct or indirect consequences of the implication of the nerves, others are independent and the result of the special action of the beriberi poison. Modern writers, regarding beriberi as a multiple endemic neuritis, give very little importance to alterations of nervous centres and other organs, and occupy themselves exclusively with the lesions of the peripheral nerves. This proceeding does not seem to me quite correct. Beriberi is first of all a general disease, *totius substantiæ;* its pathogenic microorganism acts on the entire economy, but it has an elective action on the nervous system. Post-mortem examination often reveals the existence of alterations of the spinal cord and its annexes, and sometimes of the brain. On the other hand, the analysis of symptoms shows that the exclusive implication of the peripheral nerves is not always sufficient to explain them. The symmetrical distribution of the sensory and motor disturbances, the ascending progress and the descending regression of the paralysis, the loss of memory, etc., point to the implication of the nervous centres. I believe that in beriberi, besides the lesions of the peripheral nerves, there are always more or less accentuated alterations of the nervous centres, chiefly of the spinal cord. Whether these alterations are primary or consecutive to an affection of the nerves, is a question not yet definitely settled. Nevertheless, the valuable discoveries of Ramon y Cajal concerning the neurons and their individuality sustain the opinion of those who consider peripheral neuritis as a manifestation of an affection of the central organs. In truth, it is hard to understand how a poison can attack the extremity of the neuron without affecting the rest of the organ; how it destroys the axis cylinder from the periphery to the centre, instead of affecting it at once throughout its whole extent. It rather appears that the neuron, having its vitality impaired by the toxic agent, begins to degenerate at its weakest point, that is, at the periphery which is the most remote from the trophic centres.

Diagnosis.

In localities where beriberi prevails endemically, its diagnosis is almost always very easy; experienced physicians often diagnose the disease at first sight. In places, however, where it is unknown, and in some patients residing in beriberic centres, the diagnosis becomes very difficult, and sometimes can be established only after the

disease has run its course. Inexperienced physicians, and those who are acquainted with beriberi only through the descriptions in text-books, are seriously embarrassed with the first cases observed, and often set them down as locomotor ataxia, progressive muscular atrophy, disease of the heart, anæmia, malarial fever, Bright's disease, etc. Nevertheless, the differential diagnosis between these diseases and beriberi is not difficult, and, to be made with certainty, it is sufficient for the practitioner to bear in mind the symptoms of each of these several diseases and the elements of diagnosis of beriberi. The following elements should always serve as a standard in the differential diagnosis: the previous existence of a latent neuritis; the endemic or epidemic development of the disease; the special symptoms of the initial stage, chiefly those revealed by electrical examination; the characteristic œdema of the edge of the tibia and the puffiness of the face; the irregular peripheral distribution of the sensory and motor alterations, denoted by the respective symptoms; the exemption of the sphincters of the bladder and rectum; the amyotrophy; the existence of the so-called beriberic belt; the special modifications of locomotion constituting "steppage"; the visceral symptoms, among which the most important are those of the cardiovascular apparatus; the coexistence of œdemas and effusions in the serous cavities and disorders of sensibility and motility; the progress of the disease with its stages of aggravation, pause, and retrogradation. To these several elements may be added the following: abatement of all the symptoms, and even their complete disappearance when the patient leaves the beriberic centre and takes up his residence in a more or less distant and not yet contaminated locality.

Formerly physicians, when discussing the differential diagnosis, busied themselves considerably with the analogies and differences existing between beriberi and the several forms of diffuse or systematized *myelitis*. The knowledge lately acquired concerning the symptomatology of beriberi and of myelitis demonstrates that these analogies are rather weak, and the differences radical enough not to preclude any further hesitation in establishing a differential diagnosis. The same may be said, with better reason, of hydromyelia, scorbutus, rheumatism, ankylostomiasis, and pernicious anæmia.

We cannot be so positive as regards the differential diagnosis between beriberi and *paralysis of the Aran-Duchenne type*, and *Landry's acute ascending paralysis*. It is true that in the great majority of cases beriberi exhibits clinical features very different from those of these diseases; there are cases, however, in which the symptoms are grouped and succeed each other in such a manner that confusion is not only possible but often inevitable. The verifica-

tion of the particular symptoms of the initial stage, when possible, the endemic or epidemic character of the disease, the existence of œdema and visceral disorders, and the later evolution of the disease, in case its course is not cut short by death, are indications in favor of beriberi.

Nephritis.—Brazilian physicians have called attention to the difficulties that sometimes surround the differential diagnosis of beriberi and the several forms of Bright's disease. In the third Brazilian Congress of Medicine and Surgery, Ramiro Monteiro, of Bahia, dealt with the subject in a masterly manner. The possibility of the development of a nephritis during the course of beriberi, or during convalescence from it, is no longer open to debate, whether it is consecutive to the excess of the functions of the kidneys, as Ramiro Monteiro thinks, or of microbic origin, or, as seems most probable, connected with the implication of the renal plexus. The confusion between dropsical beriberi and the acute and diffuse forms of Bright's disease is only apparent, for the examination of the urine immediately removes all doubts. It is different, however, as regards the interstitial form, in which the albumin in the urine is sometimes insignificant in amount and sometimes wanting entirely. Add to this that in the mitroaortic stage of generalized *arteriosclerosis*, besides the more or less pronounced renal disorders, there are always symptoms of cardiac weakness, and if the patient is an inveterate drinker, as often happens, sensory and motor troubles aggravate the morbid condition, rendering differentiation difficult. I have seen some of these cases, and I confess that at first sight they are of such a nature as to justify the error. A minute and accurate examination of the heart will greatly facilitate the diagnosis; in beriberi, cardiac dulness is often increased to the right; in arteriosclerosis the increase is principally to the left; in beriberi there is accentuation of the second pulmonary tone, reduplication of the second sound, and, in rare cases, galloping rhythm to the right; in arteriosclerosis, the aortic sound predominates, when not replaced by a diastolic murmur, and the frequent galloping rhythm has its maximum audibility to the left. The analysis of the urine repeated on consecutive days may also facilitate the diagnosis, revealing the presence of albumin. Besides this, the urœmic symptoms of beriberi, due to a deficient renal excretion, are never of long duration; they either disappear rapidly after a polyuric crisis or grow worse at once, and death occurs preceded by asphyxia, coma, delirium, or convulsions. The course of interstitial nephritis is incontestably slower; and the antecedents of the patient, the beginning of the disease, the way in which the symptoms progress, etc., will remove all doubts.

The differential diagnosis between beriberi and other forms of *polyneuritis* is sometimes more difficult. Brazilian physicians have dealt extensively with this subject, and the works of Nina Rodrigues, Alfredo Britto, and Ezequiel Britto may be consulted on this point with profit. The localized forms of multiple neuritis have their individual characteristics which easily prevent confusion with beriberi. The same cannot be said of toxic or infectious forms of polyneuritis, which often assume clinical features common to beriberi. In presence of such cases the practitioner should examine all the elements of diagnosis, attaching the greatest importance to the existence of an endemic or epidemic status, to the predominance of visceral symptoms, to the presence of œdemas and effusions in the serous cavities, to the previous course of the disease, to the antecedents of the patient, and finally to recovery in consequence of removal from the locality. The value of these elements, however, is entirely relative; in one beriberi district cases may be observed of multiple infectious neuritis of a yet undetermined nature, but independent of beriberi, as well as a generalized neuritis due to alcoholism, to malaria, to puerperal infection, etc.; in any of these forms of polyneuritis visceral symptoms are to be met with, as well as œdemas, and the antecedents of the patient are not always of a nature to remove all doubts. It was long believed that the occurrence of œdema was peculiar to beriberi; Dr. Nina Rodrigues expresses himself as follows: "With the exception perhaps of the generalized œdemas associated with a frank paralysis, and of the epidemic character of the disease, all other signs have only a relative value in relation to polyneuritis, and are rather distinguished by degree and extension than by quality." Dr. Alfredo Britto is still more positive when he says: "There is no confusion possible between the dropsical form of beriberi and any other polyneuritis." This opinion is too exclusive; there can be no doubt that generalized œdema is rare in the other forms of toxic and infectious polyneuritis; but medical literature mentions well-established cases which deprive that sign of much of its importance. In the patient whose case was published by Grocco the diagnosis may indeed be disputed; but in those of Gurgo and Regibus and of Dejerine and Mirallié it is free from doubt. The symptoms of the interesting case of these last-mentioned authors may be concisely stated as follows:

A man 50 years of age; peripheral neuritis of undetermined nature not beriberic; systematized motor neuritis of the four extremities, chiefly accentuated in the lower; muscular atrophy; marked alterations of electrical contractility without reaction of degeneration; general and special sensibility normal; absence of spontaneous pains;

pains provoked by pressure on the muscles and inferior members; knee-jerk abolished; absence of disorders of the sphincters; tachycardia; absence of fever; œdema of an invading character similar to anasarca; a polyuric crisis; recovery.

It is wholly impossible to establish rules and precepts for the differential diagnosis between beriberi and a multiple infectious primary neuritis, developed sporadically or endemically in a beriberi centre. Such diagnosis can be made only by attending to individual circumstances, and the practitioner will often find himself unable to do it with certainty. In the differential diagnosis between beriberi and each one of the forms of generalized secondary polyneuritis with which it has greatest affinity—alcoholic, diphtheritic, malarial, puerperal—the practitioner must make a careful analysis of all the symptoms and signs peculiar to each of these affections, and compare them with the symptoms and signs of beriberi, always bearing in mind that even the elements of diagnosis considered as the best, such as prevalence of painful symptoms and trembling in alcoholism, paralysis of the velum palati in diphtheria, the existence of intermitting accesses of fever and intermitting neuralgias in malaria, the extension and prococity of visceral disorders in beriberi, etc., are of very relative value.

Prognosis.

The prognosis of beriberi, being dependent upon manifold circumstances, is extraordinarily variable, so that it would be impossible to find a single formula capable of expressing it. Each clinical case by itself admits of a prognosis which is not the same for other cases in the same or different epidemic epochs. Add to this that, besides individual conditions, the endemic, epidemic, or sporadic character of the disease, the influence of climate, manner of living, etc., all of which exercise their influence on the prognosis, attention must also be paid to the possibility of removal of the patient away from the centre where the disease was contracted. Indeed, the prognosis is much more favorable when the patient is in a condition to undertake a journey.

The gravity of beriberi depends in part on the intensity of the intoxication, or on the greater virulence of the germs and the less resistance of the organism, but still more on the quality and seat of the nerves implicated. Patients who exhibit extreme degrees of paralysis, atrophy, or œdema may recover; in others, the disease manifesting itself by slight and apparently mild symptoms, often terminates fatally. We should not lose sight of the great liability of beriberi

patients to sudden death; it often takes place a few hours after the physician has visited the patient and observed sensible improvement. The contrary is also sometimes observed; the patient seen to-day and considered to be in a desperate state, with serious symptoms of uræmia, may be found to-morrow in excellent condition, having had during the night a polyuric crisis. P. Manson wisely says: "In the matter of death and recovery, beriberi is a disease of surprises. It is an exceedingly risky thing to venture on a prognosis in a case of beriberi."

The *mortality* varies extraordinarily, being difficult of computation. Corre, after examining a large number of statistics, established an average of 34.6 per cent. This mortality, says he, reaches its maximum among the Chinese, where it is 51.9 per cent., and falls to its minimum in Japan, where only 12.5 per cent. of the patients die; it approaches the first of these figures among the Indo-Malays, and especially among the Brazilians, perhaps owing to a mixture of negro blood. This opinion of Corre is not correct in relation to Brazil. It is true that the first statistics collected by Silva Lima, referring to the period 1863–1871, exhibited a high mortality—above 50 per cent. From 1872 to the present date, however, either because the disease has become milder or because the treatment has grown better, the mortality has diminished considerably. Even so, it varies largely from one year to another, and from one place to another. In the Marine Hospital of Rio de Janeiro, for instance, from 1869 to 1875, the average mortality was 13.5 per cent. In a special hospital established for beriberics at Nova-Friburgo, 231 patients were treated in 1889, of whom only 5 died, which is a little more than 2 per cent. On the other hand, in the beriberic hospital of Copacabana (Rio de Janeiro), 391 patients were treated in 1896; of these 101 died, which corresponds to a mortality of 25.5 per cent.

Treatment.

No specific medical treatment is yet known for beriberi. Many drugs have been tried; some even have enjoyed a certain reputation for a time; clinical observation, however, has shown that no confidence is to be placed in any of them, and that their use is rather harmful than advantageous. The only really efficacious remedy in the treatment of beriberi is the removal of the patient away from the place where the disease was contracted. This should be done as soon as possible. The patient should either go to a high and dry locality, where beriberi is not endemic, or undertake a sea-voyage. Removal is so efficacious that it produces a good effect even when the patient

goes to an unhealthy place where the climate is bad, provided beriberi is not endemic there. The statistics of mortality of beriberi in Brazil afford the most convincing argument in favor of removal. From 1863 to 1866 in Bahia, before patients had begun to adopt this course, the mortality was, according to Silva Lima, 74.5 per cent. From 1869 to 1875, the mortality among the beriberics removed from Bahia to the Marine Hospital of Rio de Janeiro, where beriberi did not yet exist, was only 13.5 per cent. After beriberi became endemic in Rio de Janeiro, the mortality in this city rose to 25 and 30 per cent.; but among the patients removed from Rio de Janeiro to the special infirmary at Nova-Friburgo, it reached only 2 per cent. These figures are significant enough to impose upon governments the duty of establishing special sanatoria in high and dry places, free from beriberi, where persons suffering from it may be treated; and, if there is careful vigilance on the part of the physicians of military garrisons and ships, and of the directing and medical *personnel* of prisons, asylums, schools, etc., to the end that individuals exhibiting the first symptoms of the initial phase of beriberi may be promptly removed to the sanatorium, it may be confidently expected that the mortality of this disease will be much reduced and almost suppressed.

When removal is impossible, care should be taken to place the patient in a well-ventilated room. He should be removed from the neighborhood, from the house, or at least from the room, in which he was taken ill. The patient should be surrounded with all hygienic conditions, including such good and substantial diet as his stomach will bear; if he can go out in the fresh air without excessive fatigue, he should be encouraged to do so as much as possible, avoiding, however, long walks and exposure to the sun or to the damp, which are always hurtful.

The use of drugs in the treatment of beriberi should be the most simple possible, obeying the indications created by symptoms exhibited by the patient, or rather by the morbid elements that enter in the constitution of the disease. Prompt and energetic intervention should be used to combat morbid elements, which, by their continuance and progress, might threaten the life of the patient, such as cardiac asthenia, dyspnœa, dropsy, uræmia, etc. In the treatment of beriberi the practitioner should pay particular attention to the condition of the heart; the work to be performed by this organ almost always increases, owing to the pulmonary lesions; it is proper, therefore, for the physician to come to its aid, in order to prevent its becoming weakened. I prescribe systematically digitalis or digitalin to all beriberics presenting an increase of cardiac dulness to the right and accentuation of the pulmonary second sound. When the patient

shows signs of acute dilatation of the right ventricle and sudden weakening of compensation, together with symptoms of rapid asystole, digitalis or digitalin is inefficacious, because it has not time to act; something must be done at once, and the best means of strengthening the heart is to diminish its labor at first, which is effected by a general blood-letting of 300 or 400 gm., followed by hypodermic injections of caffeine or camphorated oil. After the cessation of the acute stage, the dangerous symptoms having disappeared, the use of digitalis may be resumed. This same treatment gives also the best results when there is intense dyspnœa due to uræmic intoxication or acute œdema of the lungs. In the latter case, besides the general blood-letting, the wall of the thorax and the region of the liver should be scarified and cupped, and cups should also be applied to the extremities.

The beneficial and almost miraculous effect of blood-letting in those cases in which death is imminent has led some Brazilian physicians to employ it systematically in all cases of beriberi, whatever be the symptoms exhibited by the patient. This practice is not to be imitated, and can only lead to disastrous consequences.

In dropsical and mixed beriberi, when there is a diminution in the quantity of urine voided daily, with symptoms of slight uræmia, drastic purges are advantageous, specially when accompanied by heart tonics and diuretics. In these cases I prescribe either compound tincture of jalap, or calomel, or elaterium; I repeat the purge once a week; I keep the patient on an absolute milk diet, and prescribe 2 gm. of theobromine and a potion composed of 60 cm. of powder of digitalis leaves, to be taken every day after the purge. The other heart tonics, chiefly strophanthus and sparteine, are often successfully employed.

The physician will sometimes be compelled to have recourse to other drugs in order to combat troublesome symptoms, such as pains, cramps, gastric disorders, etc. Some physicians adopt the systematic use of nux vomica, strychnine, phosphide of zinc, ergotin, iodide of potassium, or arsenic, in order to overcome beriberic paresis. I think these remedies rather hurtful than beneficial, especially when employed at the outset of the disease and during the progressive stage of the paralysis. I may say the same of physical agents—electricity, massage, hydrotherapy. Nevertheless in chronic cases, or in regressive stages of the disease, after the acute aggravations have ceased and the paralysis begins to yield, the use of these physical measures, sea bathing, electricity, massage, and the employment of general tonics are indicated, being always followed by good results.

Prophylaxis.

The prophylaxis of beriberi is a subject worthy of the attention of physicians and of governments; it demands the execution of measures very similar to those employed against other infectious diseases. Though doubts may still exist concerning the mode of transmission of beriberi, whether by direct contagion or by simple infection of the soil and passage of germs into the atmosphere, the reality of transmission is no longer subject to contestation, and therefore the necessity of avoiding it is indisputable. In an epidemic season patients, when possible, should be removed to special hospitals and infirmaries, rigorous disinfection should be carried out in the houses and rooms where the patients have been, as well as in the neighboring soil. Whenever a beriberic is to be removed to a locality where the disease does not exist, he should, before leaving, take a general bath and his clothes and effects should be rigorously disinfected. In jails, schools, asylums, and other collective habitations, during an epidemic, the inmates should be periodically examined, and those exhibiting the first symptoms of beriberi should be removed to a healthy locality. These large buildings shall be frequently disinfected, for which a solution of corrosive sublimate in the proportion of one or two parts to a thousand, and a steam pressure apparatus (Geneste-Herscher, for instance) may be used.

Besides these defensive prophylactic measures, which should always be executed in endemic centres during an epidemic, measures of aggressive hygiene must not be forgotten. Damp localities must be drained and hygiene of the soil and of dwellings must be carefully attended to. At the same time agglomerations of peoples in collective dwellings must be avoided and the inmates of these habitations must be provided with good food.

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MILIARY FEVER.

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MILIARY FEVER.

MILIARY fever is an endemoepidemic affection almost exclusively confined to certain regions of France, Italy, Germany, and Austria; it is a disease of very variable gravity; its chief symptoms are profuse sweating, a peculiar eruption, and certain special nervous phenomena.

We shall study successively the geographical distribution of the disease, its clinical characters, etiology, and mode of transmission, and its epidemiological peculiarities. We shall then occupy ourselves with the relations of the affection with the formidable epidemics described under the name of "English sweating sickness" (*suette anglaise*), which we believe to have been identical with miliary fever. This last part of our study seems to us to present a special interest at this time in connection with what we are witnessing in regard to the plague. We have just seen the formidable expansion of an endemic of this disease, the outcome of which we are unable to foresee, arising from an endemoepidemic centre to which we had supposed that it was definitely confined. We may well ask, in view of this fact, whether the human race may not at some time be concerned with the recrudescence and spread of this sweating sickness, the ravages of which are described so graphically by the chroniclers of the sixteenth century.

The most important of the works which have been consulted in the preparation of this article are indicated by their titles in the section on Bibliography below.

Synonyms.—Purpura, purpura alba, febris miliaris; French, *suette miliaire, fièvre miliaire;* German, *Hirsefieber, Friesel.*

History.

According to Allioni and Seitz miliary fever appeared first in Leipsic in 1652, when it was described by Hopp and Welsch. It next appeared in Augsburg in 1660, and after that at frequent intervals in various parts of Germany. Sydenham described its occurrence in London in 1684, and its existence in England was noted several times up to 1741. The first epidemics noted in France were

those of Montbeliard in 1712 and of Abbeville in 1718. Switzerland, Italy, Denmark, Sweden, and Russia were also visited by epidemics of miliary fever in the course of the last century.

At the present time miliary fever is encountered chiefly in France, where it occupies a certain number of centres which appear to have no relation one to the other. The following are the most important of these foci: In the north of France we find it in the department of Somme and the neighboring departments of Oise, Aisne, Seine et Oise, and Pas de Calais. This is the "suette de Picardie," the first description of which we owe to Bellot. The same endemic prevalence, this time chiefly in the departments of Oise and Seine et Oise, was the object of an excellent study by Rayer in 1821. In the west we find the disease in the departments of Dordogne, Charente, Charente Inférieure, Vienne, and Deux Sèvres, which are the centres of the "suette perigourdine" and the "suette poitevine." It was the outbreak in this last centre in 1887–88 that brought the disease into special prominence in recent years. Less important foci have been noted in the centre of France in the departments which correspond to the ancient province of Auvergne, in the south in the departments of Aude, Hérault, and Var, and in the east in Franche Comté and Dauphiné and in Alsace and Lorraine. There are, indeed, few departments in France which have not at some time been visited by this disease. Normandy, which has enjoyed an almost absolute immunity during the nineteenth century, was often visited during the past century. Brittany alone seems always and permanently to have been free from the affection.

Outside of France miliary fever has been observed in the course of the present century in Italy, in Piedmont, Lombardy, Venice, and Liguria. In Germany it has been noted in the southern part of Bavaria, in Würtemberg, and in Baden. It has been observed only exceptionally in the northern part of Germany. In Austria an epidemic was noted by Drasche and Weichselbaum in Carniola in 1892, and in 1893 the presence of the disease was reported in Styria. The affection has also been observed in the present century in Switzerland, Belgium, and Spain.

Symptoms.

We cannot better begin the clinical study of this disease than by reproducing the classical picture which Rayer has left us. "The invasion of the disease was sometimes announced by a slight feeling of lassitude, pain over the eyes, and loss of appetite. Frequently also the invasion occurred without any precursory signs. Many persons who had gone to bed feeling well awoke with the disease upon

them, the body being bathed in a profuse sweat which persisted until death or convalescence took place. Sometimes a slight, scarcely perceptible, febrile movement occurred, or there was a burning heat, or a sensation as of vapor passing through all the limbs; and almost always a feeling of compression at the epigastrium preceded by one or several hours or by a few moments only the appearance of the sweat, or rather of the warm vapor, which was at first limited to a certain part of the body and then spread over the entire surface. The mouth was pasty, the tongue was covered with a dirty white, rarely yellowish coating, the thirst was very great, but there was little or no desire for food. The urine often seemed to be normal. Constipation was usually present throughout the entire course of the disease. The pulse was normal in many cases, but became frequent and fuller at the time of the eruption. There was the same kind of impediment or embarrassment to the respiration that is experienced in a place where the temperature of the atmosphere is too high. The head and the organs of special sense and of generation remained free from the disorders and sufferings experienced in other parts.

"This state persisted with slight variations during the second, third, and fourth days of the illness. It was on one of these days, usually on the third, that there appeared on the skin, after a slight pricking sensation, an eruption of red conical miliary papules, the tips of which sometimes became white before the eruption disappeared. Between these red papules, or on other parts of the body, but rarely over its entire surface, appeared a few pearly lesions or vesicles of a rounded shape and filled at first with a clear serous fluid.

"The eruption, whatever its form, was preceded by a pricking and itching of the skin. It lasted only two or three days, except when it recurred in irregular and successive paroxysms. Sometimes it was followed by considerable desquamation of the epidermis. In other less frequent cases, whether the disease had been left to itself or had been modified by more or less active medication, no eruption took place, the only symptom being the persistent sweating, accompanied or not by itching.

"All these morbid phenomena gradually disappeared from the seventh to the ninth or tenth day after the initial symptoms."

We have quoted here the description given by Rayer of the disease as it appeared in the epidemic of 1821. We find in this picture all the symptoms of miliary fever, which are seen to be few in number, the principal of them being sweating, an eruption, and nervous phenomena. We shall now study each of these separately.

The Sweats.—These constitute the most constant of all the symptoms, although Landouzy and Guéneau de Mussy have reported a

case in a child in which sweating was absent. Foucart, indeed, says that these cases are quite common, and he describes a form of miliary fever without sweating or eruption, characterized solely by nervous phenomena and gastric symptoms.

The sweating appears with the beginning of the disease and continues throughout its entire course, flowing, or rather exhaling from the skin in the form of a heavy vapor. These sweats are so abundant that in certain patients it becomes necessary to change the linen ten times in the twenty-four hours or even more frequently. Riedel reported a case which came under his observation at Hallendorf in 1888, in which the linen was changed sixty times in the course of three days; the patient recovered.

The sweats are continuous, the patient is always wet with perspiration, but there occur exacerbations from time to time, constituting veritable sudoral paroxysms.

Rayer speaks of a peculiar fetid character of the sweat, recalling the odor of decaying straw. Parrot, Foucart, and Brouardel explain this odor as an evidence of want of cleanliness of the patient, consequent upon the popular prejudice against changing the linen and also against ventilating the apartment, which those having the care of the patient keep tightly closed.

Eruption.—The eruption appears usually in the evening of the third day of the disease or during the night between the third and fourth days. It is ordinarily preceded by a sensation of formication. It appears first on the sides and back of the neck, in the axillæ, and, in women, under the breasts. It is then noted successively on the back, the internal surface of the arms, the abdomen, and the inner surfaces of the thighs and legs. It sometimes develops with considerable rapidity, the entire surface of the body being covered in the course of twenty-four to thirty-six hours; but at other times its evolution is much more gradual, occupying several days, so that it may be drying up or have already disappeared in certain parts while it is only beginning on others. It may appear in successive crops.

Rayer distinguishes several forms of eruption: 1. Miliaria rubra, a miliary exanthem occurring under the form of little hard, red, conical granulations which are surrounded by a red area of the skin. 2. Miliaria alba, in the form of small transparent vesicles which at first can be seen only by stretching the skin and looking at it obliquely; they are then visible as little pearly granulations, rather resembling transparent droplets, over which, however, one may pass the finger gently without removing them. 3. Miliaria phlyctenoides, in the form of phlyctenulæ of irregular shape, sometimes convex and sometimes flattened on the surface, the area of which is often as large as a

lentil or even larger. 4. Minute yellowish points which can be distinguished under the epidermis on the palms of the hands and soles of the feet where the skin is thick. Of these four forms the red miliaria was the most commonly encountered, although in many cases the others existed at the same time, and in some instances even were present alone to the exclusion of the others.

In fact, however, Rayer's description does not give a very accurate idea of the eruption, or rather it gives an exaggerated importance to secondary elements while according second place to the essential primary element. His miliaria alba is nothing really but sudamina, the presence of which is of no significance whatever, indicating only the occurrence of a profuse perspiration. The miliaria phlyctenoides results from the confluence of the sudamina, which after a little while may present a cloudy or even purulent appearance. The miliaria rubra is merely a very slight papular eruption which may later become transformed into a vesicular eruption.

The essential and primary element of the eruption of miliary fever is the *erythema*, which all authors have described as serving for a substratum for the other eruptive elements, and which is described as follows by Rayer: "The skin presents a red shagreened appearance, and accompanying this is a notable tumefaction of the arms, forearms, and back of the hands." This erythema may assume various types, among which we distinguish the rubeolous, in which the patches of eruption are scattered in variable number over the cutaneous surface; and the scarlatiniform, in which the skin has a uniform red tint. This scarlatinal appearance is often secondary and results from the confluence of the rubeolous patches. There may also be here and there little purplish spots which cannot be distinguished from the rest of the eruption by the finger; this constitutes the hemorrhagic form, and is quite rare. The exanthem is especially marked on the trunk and upper extremities. In the epidemic of 1821 it always spared the face, while in that of 1887 this part was always affected.

The mucous membranes may also participate in the eruption. Barthez, Landouzy, and Guéneau de Mussy have noted the presence of miliary vesicles on the velum and vault of the palate. Foucart has seen disseminated red patches on the inner surfaces of the cheeks, the palatine vault, and the velum palati.

The appearance of the eruption is preceded by a pricking and itching of variable intensity. It disappears gradually and is usually followed by desquamation, occurring in limited patches (*desquamation en collerette*) or in great sheets (*desquamation écailleuse* or *en doigt de gant*).

That lesion which has been regarded as so important as to give its name to the disease, that is to say, the miliaria, is not an absolutely constant phenomenon. Rayer said that it might be absent, and we shall have occasion to insist more particularly on this fact when we come to study the relations of miliary fever to the English epidemics of sweating sickness during the Middle Ages. It is very possible, however, that in many cases in which this eruption was said to be absent, the patients were not examined with sufficient care.

Nervous Phenomena.—These form, with the sweats and the eruption, the classical triad of symptoms of miliary fever. The most common and the most characteristic among the symptoms of this class is the feeling of constriction at the epigastrium which is noted in all cases and in all epidemics. This oppression is often so great and the anxiety which accompanies it so distressing that the patients have a sensation as of constantly impending suffocation. This phenomenon appears at its maximum at the time the sweats come on and presents exacerbations when the eruption appears, and also with each new eruption when this occurs in successive crops. The feeling of oppression is absolutely independent of any change in the thoracic organs, the most careful examination of the chest revealing nothing abnormal in the lungs even when the patient is struggling for breath, sighing, and obtaining a measure of relief only by means of the deepest inspirations. The heart is also found to be perfectly normal even when the patients complain of violent palpitations and when an inspection of the epigastrium reveals a marked pulsation in this region. This cardialgia, which appears to have been specially marked in the epidemic of Röttingen, is sometimes atrocious. The patients occasionally complain of a sensation as if the heart were suspended by a thread in the chest.

Foucart dwells especially upon a sensation of constriction in the pharynx, the patient complaining of a most distressing feeling of strangulation.

Alongside of these special nervous symptoms, which we find in equal intensity and with equal frequency in no other disease, we may mention some others which are less constant and which are moreover common to all febrile affections. These are a general malaise, weakness, muscular fatigue, headache, articular pains, vertigo, and insomnia. Delirium has been noted in a rather large number of cases. According to Rayer this is of an active character, and it is accompanied by a congestion of the face, bulging eyeballs, and throbbing temporal arteries. In some cases the patients succumb in a few hours in a condition of coma following upon a furious delirium, or with evidences of paralysis.

Convulsions have been observed in the period preceding the appearance of the eruption. These convulsions are tonic in character, limited in extent, and temporary only, and in this case they have no special prognostic significance; but when they are more or less generalized they often precede by a short time only a fatal termination of the disease.

The nervous phenomena as a rule subside gradually after the appearance of the eruption and disappear entirely with the other symptoms of the malady. Sometimes, however, some of them persist for a longer or shorter period after convalescence has been established. Among these persistent phenomena have been noted attacks of intercostal neuralgia, rectal crises analogous to those of locomotor ataxia (Thoinot), and mental troubles.

Temperature.—Fever is present in the stage of invasion, lasting up to the appearance of the eruption. It varies in degree according to the intensity of the attack, reaching 40° or 41° C. (104°–105.8° F.) in very severe cases. In certain epidemics the disease has begun with a long-continued and violent chill followed by insatiable thirst and a dry tongue. In other epidemics this mode of origin has been less pronounced. Some fever is the rule in all cases. In fatal cases Mazuel has seen the temperature rise to 42° or 43° C. (107.6° to 109.4° F.) just before death.

Digestive Apparatus.—Indigestion is frequent. Foucart says that it is the rule, constituting one of the most important symptoms and furnishing one of the capital indications for treatment. The indigestion is manifested by the pasty condition of the mouth, a thick white coating on the tongue, a slight epigastric distress, anorexia, great thirst, nausea, and sometimes even vomiting of food and bile. These symptoms frequently precede the sweats and constitute a prodromic stage of the disease. After the appearance of the eruption the phenomena are modified somewhat, and there is a desquamation of the tongue similar to that of the cutaneous surface. This desquamation is analogous to that in scarlet fever, and is usually partial only.

Constipation is common during the continuance of the disease. In the epidemic of 1887, there was noted the occurrence, after the appearance of the eruption, of numerous stools of the consistence of pea soup or of tar, and having a very foul odor (Thoinot).

The Urine.—Parmentier has made a careful study of the variations occurring in the quantity of urine voided at various stages of the disease. He found that the urine is considerably diminished in amount in the third, fourth, and fifth days, the amount being from 200 to 400 gm. (6 to 12 oz.). From about the seventh day the quantity excreted insensibly increases up to the ninth or tenth day. From the tenth,

thirteenth, or fourteenth day, when the sweats ordinarily disappear completely, an increase occurs in the amount of urine. This sometimes takes place very suddenly, the quantity rising rapidly to the normal or surpassing it, reaching two or three litres (quarts). This sudden increase in the quantity of urine excreted constitutes a urinary crisis marking the beginning of convalescence.

Rayer has noted the occurrence of vesical tenesmus in the early stage of miliary fever. He says that the urine preserves its usual color, but most writers have mentioned a reddish color and an abundant sediment such as we see in other febrile affections. There is never any albumin or sugar in the urine. Parmentier says the proportion of urea is diminished at the beginning, but increases at the time of the crisis accompanied by polyuria.

Genital Functions.—Rayer has stated that the genital functions in woman were in no way affected during an attack of miliary fever. Barthez, Landouzy, and Guéneau de Mussy say that the only changes occurring in menstruation are of a very insignificant character, but Parrot, on the other hand, regards the influence of the disease in this function as a very marked one. The disease, he says, hastens the appearance of the menstrual flow or brings it on even when it is not due, and it also causes premature delivery or abortion in pregnant women. Indeed, he remarks that miliary fever is a true emmenagogue. This was observed in marked degree during the epidemic of 1887. In this epidemic Parmentier saw nine pregnant women, of whom five died, two aborted, and two recovered without aborting. Miliary fever does not arrest the secretion of milk in nursing women.

Respiratory Apparatus.—We have seen above that the lungs are usually normal, and that the oppressed and anxious respiration is a purely nervous symptom. In the epidemic of 1887, however, cough was rather frequent, and was noted before the eruption in children who quite commonly had coryza following it. In some patients a bronchitis of slight gravity occurred during the period of eruption.

Circulatory Apparatus.—The blood is seldom altered in miliary fever beyond the fact that it presents the characters of a moderate anæmia.

There are no lesions found in the endocardium or myocardium after death, though the irregular pulse and arrhythmia noted in many convalescents would seem to point to some affection of the myocardium. Parrot insists especially upon the constancy of the epigastric pulsation. The frequency of the pulse is in direct relation with the elevation of temperature.

Hemorrhages are not uncommon, especially epistaxis which, ac-

cording to Orillard, is of grave prognostic significance. Parmentier observed intestinal hemorrhage in five patients who recovered.

Palpation of the spleen shows no increase in size.

Course, Duration, Termination.

The evolution of miliary fever may be divided most simply into three periods, viz., the pre-eruptive period, or the period of invasion, the period of eruption, and that of convalescence. The period of invasion, the beginning of which is brusk, lasts usually three or four days. Its chief symptoms are sweating, fever, general weakness, and the nervous phenomena already described.

The eruption is announced by itching of the skin, and especially by an increase in the intensity of the nervous symptoms, such as agitation, distressed breathing, epigastric constriction, and palpitations. As soon as the eruption has appeared all the symptoms become moderated; the eruption, indeed, seems to constitute a crisis which affords relief to the patient. Frequently the eruption appears in successive crops, each one preceded by an exacerbation of the symptoms; there may be two, three, or four of these recrudescences followed by a new eruption.

Convalescence is established slowly and progressively. The eruption fades out, the fever declines, and the patient begins to ask to be allowed to get out of bed. This occurs usually in the second or third week, but the complete return to health is slow and difficult. The loss of flesh is marked and rapid. "One is actually astonished to see a man, who a week before had a large abdomen, become almost thin in such a short space of time" (Rayer). For a month or more the patient's complexion is of a yellowish earthy color. He is incapable of resuming his ordinary avocation before the end of several weeks. Sometimes there is œdema of the lower extremities, especially of the feet. There are fibrillary twitchings of the face, the tongue is tremulous like that of a general paralytic. The patient complains of very persistent insomnia and anorexia, and when the least overfatigued he perspires profusely. Some convalescents have cardiac arrhythmia, others continue to suffer from the neuralgia which they had during the course of the disease. This difficulty, this slowness, and this uncertainty of the convalescence are quite characteristic of miliary fever. They are seen after even very mild attacks. Bucquoy, of Peronne, has reported cases in which a complete return to health was delayed one or two years.

All who have described epidemics of miliary fever have referred to the possibility of relapses during the period of convalescence.

These relapses appear to have been particularly frequent in certain epidemics. The symptoms of the relapse are the same as those of the primary attack. The evolution is also the same except that it ordinarily proceeds with greater rapidity. The relapse is seldom fatal; Parrot did not lose one of his patients who suffered a relapse. We are wholly ignorant of the cause of these relapses, for such as have been observed could not be attributed to an imprudence in diet or to any other definite fact.

The usual termination is in recovery, but death is possible, and even quite common in certain epidemics. The fatal cases generally progress with great rapidity, giving one the impression of unusual malignancy and perniciousness. Parrot speaks of fatal cases in which death occurred in from three to eight hours after the onset of the disease. Rayer reports cases in which death occurred in fourteen, thirty, and forty hours. Barthez has seen other cases terminating fatally within twenty-four hours, and Keesbacher in 1873 noted instances in which death occurred in ten hours. These foudroyant cases which kill at the appearance of the eruption are marked especially by the great intensity of the nervous symptoms. The feeling of oppression is extreme, and the patient suffers from an indescribable feeling of malaise which is comparable only to that of impending death. He may fall as if struck down by a blow, and sometimes loses consciousness at once. Ordinarily, however, coma does not come on with such extreme suddenness, but is preceded by a period of delirium and convulsions. The face is congested, the eyes are prominent and congested, and the pupils are contracted and immobile. In other cases death is not absolutely sudden, but can be characterized simply as rapid, the patient succumbing after twenty-four to forty-eight hours.

In still other cases the onset of the disease presents nothing peculiar, and all the symptoms seem to point to the occurrence of a mild case; but on the second, third, or fourth day, when the eruption is about due, the affection takes on features of malignancy. The fever rises, the sweats soak the patient's bed, the feeling of suffocation grows more intense, and expansive and noisy delirium appears. Complaint is made that the epigastrium feels as if in the grasp of a vise, and in the course of a few hours the patient succumbs.

These accidents may supervene even after the appearance of the first eruption and just as a new crop is on the point of coming out. Recent observations have shown that cases of this sort are accompanied by hyperpyrexia.

Varieties.

Taking the intensity of the symptoms as a standard, miliary fever has been divided into benign, grave, foudroyant, and ambulatory. On the base of undue prominence of one or the other of the symptoms the cases have been grouped into inflammatory and gastrointestinal. A study of the epidemic of 1887 has brought out a peculiarity of miliary fever when occurring in young subjects, in that the eruption and general symptoms are similar to those of measles, and infantile miliary fever has, indeed, often been confounded with measles.

Miliary fever may run its course without eruption according to Borsieri, Rayer, and others, though Foucart doubts the existence of such forms. On the other hand, this author admits the existence of miliary fever without sweating of which Pujol had already observed several cases.

Parrot, in describing the epidemic of Dordogne, and Tauflieb, in his report of that of Bas Rhin, remark especially on the frequency of the remittent or intermittent form of miliary fever. In these cases the exacerbations are marked by a noticeable increase in the frequency of the pulse, by a greatly marked precordial anxiety, and increased cephalalgia and delirium.

Diagnosis.

In a country where miliary fever is endemic and where consequently one always thinks of the possible appearance of the disease, diagnosis of the affection is usually not difficult. The disease has its special character, and a peculiar association of essential symptoms. Certain authors who regard the sweating as the essential symptom of this disease have occasionally confounded miliary fever with all sorts of miliary eruptions associated with sweating, especially those which may complicate scarlet fever or puerperal septicæmia. The Vienna dermatologists and also certain Italian physicians, directing attention especially to cases in which this confusion has occurred, have gone so far as to deny the existence of any specific sweating sickness.

Brouardel and other members of the committee sent to observe miliary fever in Vienne in 1887 insisted especially on the differential diagnosis of the rubeolic form of the disease from measles. This diagnosis is very easy when we are in position to watch the disease from its inception. Rubeola has a long and definite period of incubation; it is not accompanied by sweating or by the nervous phenomena peculiar to miliary fever. The character of the eruption also differs in the two diseases. In miliary fever the skin gives a shagreen

feeling to the hand as it is passed over it, and under a lens the vesicles can easily be made out. In miliary fever the catarrhal symptoms are very slight or absent altogether. A history of a previous attack of measles will be of assistance in doubtful cases.

The diagnosis from scarlatina, the eruption of which may be simulated by that of miliary fever, is usually comparatively easy, easier indeed than that from measles.

Prognosis.

Few diseases present such marked differences in the gravity of their course as does miliary fever. In certain epidemics there are scarcely any deaths, while in others the fatality is as great as that accompanying any of the most malignant of affections. We find a most striking contrast between the epidemics in which Foucart treated 1,455 cases without a single death, and that of 1852, in which Bernay recorded 16 deaths in 26 cases, a percentage of 61.5. In 1887 we find the extreme figures of 33 per cent., 1.33, and even 0 per cent. The epidemic of 1485 was marked by a fatality of 99 per cent., while that of 1506 was so much less murderous that no deaths at all occurred among those who were properly taken care of. In the same epidemic also, as in that of 1887, the mortality may vary greatly in different localities.

Miliary fever is, however, an essentially treacherous affection, and there is no symptom upon which we can rely for a prognosis; indeed, we can never promise a cure even when the symptoms are of the mildest character (Parrot). "Si cautus fueris non fides signis etiam melioribus" (Bellot).

By taking the average mortality of a certain number of epidemics between 1847 and 1868, Léon Colin obtained the percentage of 13. The following are the mortality rates recorded in the epidemics mentioned: Oise (Rayer, 1821), 5 per cent.; Seine et Marne (1839), 12; Dordogne (Parrot, 1841), 8; Austria (Keesbacher, 1873), 3; Bavaria (Riedel, 1868), 22; Haute Vienne (Brouardel, 1887), 4; Austria (Drasche, 1892), 24.

As a rule the grave cases are more numerous at the beginning of an epidemic than at the close. Miliary fever is particularly apt to be benign in children.

Pathological Anatomy.

No progress has been made in our knowledge of the pathological anatomy of miliary fever since Rayer's time. Contemporary authors have found nothing at autopsy beyond injection and extravasations

in the stomach and trachea. Drasche and Weichselbaum have noted the presence of ecchymoses under the endocardium. These authors, as well as Parrot before them, found the spleen enlarged and softened. The bacterioscopic researches of Weichselbaum in 1891, as well as those undertaken in France in 1887, have given negative results.

Treatment.

We shall defer the discussion of the prophylactic treatment of miliary fever until we have studied the mode of transmission and the epidemiological conditions of the disease.

The curative treatment of the sweating sickness has been the object of numerous investigations by different authors, but the results obtained have been of the most diverse character. All, or almost all those who have written of the disease, however, have united in opposing the treatment by means of sudorifics, which is popular among the peasants, and which is, according to Foucart, the principal cause of an unfavorable termination. According to this method the patients are kept in bed under several coverings, and even in midsummer the windows are hermetically sealed and the doors are kept most carefully closed. Not content with this, the patients are inundated with immense quantities of aromatic infusions taken as hot as they can be borne.

The proper management is, on the contrary, to cover the patients as lightly as possible, to leave the windows open even at night, and to remove the wet clothes frequently and to replace them with dry ones. These hygienic measures are productive of the greatest comfort to the patients

Bleeding, which was recommended by Rayer, has long since been abandoned.

Because of the symptoms of gastric distress Foucart and Jules Guérin have advised the employment of emetics. Jules Guérin regarded ipecac as the best drug for this purpose, and Foucart attributed to this the fortunate recovery of all his patients. He gave an emetic at the very beginning of the disease, and repeated it whenever the nervous phenomena manifested a certain degree of intensity. In addition to the emetic Foucart gave a saline purgative, usually on the third day.

During the epidemic of Dordogne, Parrot expressed himself as much pleased with the results of the employment of sulphate of quinine. This drug was also highly spoken of by Tauflieb, but it does not seem to have been used during the epidemic of 1887, in which the treatment was almost purely expectant, the only

measures employed being cold affusions, the wet sheet, or cold packing in cases of hyperpyrexia accompanied by marked nervous symptoms.

Epidemiological Study.

The territory occupied by an epidemic of miliary fever is of very variable extent. We have accounts of epidemics limited to a village or even a part of a village, others occupying a canton, an arrondissement, a department, or an entire province. The population exposed to the epidemic varied, therefore, from ten or a dozen individuals to a hundred, a thousand, a hundred thousand, or even more, according to the case. Among the epidemics of greatest extent we may cite that which in 1782 caused 31,000 deaths in Languedoc; that of 1821, which attacked 60 communes in Oisé; that of 1832, which attacked 82 communes in the same department of France; that of 1841–42, which prevailed in the departments of Dordogne, Charente, Lot et Garonne, Deux Sèvres, and Tarn et Garonne; that of 1849, which was spread over Somme, Oise, Seine et Oise, Aisne, Marne, Meuse, Meurte, and Yonne; and that of 1887 in Vienne, Indre, Haute Vienne, Deux Sèvres, and Charente. In 1849 there were several centres of miliary fever in France which were separated one from the other; besides the northern departments above mentioned, the disease was seen in the Deux Sèvres and Haute Vienne, in Gers, and in Puy de Dôme.

The duration of the different epidemics in any one locality also varies considerably. It lasted but a very short time in the localities visited in 1841–42—only eight days in one place and a month in another. In the epidemic of 1821 Rayer noted that the duration varied in different localities from seven to one hundred and sixty-five days. The duration of the disease in any one commune was seen to be shorter the farther removed this was from the primary centre of infection. The appearance of new foci of infection generally occurs progressively. Sometimes we may follow the progress of the disease very certainly, the affection seeming to start from one localized centre, in which miliary fever occurs from time to time sporadically, and then to diffuse itself little by little and equally in all directions. More often, however, the disease advances along a single line which may wind about in the oddest sort of a fashion, even sometimes turning back on itself. It was in this way that the disease advanced in Dordogne in 1841, Parrot believing that it followed the direction of the wind, which was from the southwest.

We are wholly ignorant of the reasons for the very marked differences as regards the extent and the duration of the several epidemics

of miliary fever, but there are no grounds for assuming that the direction of the wind is of any importance, as Parrot supposed. We believe, on the other hand, that contagion plays the most important if not the only rôle in the propagation of the affection and in the migration of epidemics.

In 1812 Schahl and Hessert, describing an epidemic which was prevailing in the department of Bas Rhin, noted that the disease was imported into Rosheim by prisoners brought there from Schlestadt, and they followed the further progress of the epidemic in connection with certain individuals whose wanderings they described. They advised isolation as the best means of opposing the spread of miliary fever. In Rosheim with a population of 3,730 souls there were 300 who suffered from miliary fever. Among the Jews of the city, who numbered 750, there were no cases at all, and on investigation it was learned that the members of this community made it a practice to avoid all houses where people were known to be ill with the sweating sickness.

Rayer, although not daring to venture a positive opinion, cites a number of facts pointing to the influence of contagion. Several villages were invaded after the arrival of persons who had been in infected localities and who were themselves the first attacked. Fairs and markets were in many instances important agents in the dissemination of the affection. Finally, in infected regions, those persons who kept themselves absolutely aloof from all others suffering from miliary fever escaped the disease. However, Rayer also reports several cases in which persons escaped although they had been in close contact with those affected.

Parrot, Gaillard, Foucart, and others do not believe in direct contagion.

Loreau, in 1845, observed a number of very convincing instances of direct transmission of miliary fever from the sick to the well, the most curious of which was the case of a lady who lived at a distance of 25 km. from Poitiers in a village where the disease had not yet declared itself. This lady came to Poitiers to attend the funeral of her brother, who had died of the prevailing disease, and two weeks later she herself came down with the same. The son of this lady's farmer was seized a fortnight after his mistress, and his two sisters became affected after nursing him. The priest of the village came to administer the last sacraments to the lady, and that very evening he became ill, and six days later was dead. The physician who attended these patients also was attacked in his turn.

The epidemic of 1887 furnished a large number of similar facts, and all those who have written of this epidemic have declared them-

selves strong believers in the contagion theory. Drasche and Weichselbaum report the two following cases observed by them in the epidemic of 1892. The epidemic appeared first at Gradische, and the first patient at Gurke was a man who had worked at Gradische and had returned from that place ill. The next two to suffer from the disease were the sister and the mother of this man. In another place a woman died of miliary fever on April 15th. Her three sisters living in the same village, but in different houses, were the next to be attacked; they had visited the first patient and had performed the last offices for her.

In a certain number of cases even we are able to gather facts of service in the study of the duration of the period of incubation of miliary fever. This period varies within rather wide limits. It is usually very short, twenty-four hours or less, but in a case observed in 1827 and cited by Brouardel, it was apparently not less than two weeks. One of the most conclusive observations was made in 1893 during an epidemic at Aussee in Styria. A young girl who had been among the ill went to Vienna, where she remained fourteen days she was seized with miliary fever while in the wagon on her way back from Vienna to Aussee.

Although these facts would appear to establish conclusively that miliary fever is spread by contagion, we are still absolutely in the dark as to the vehicle of the contagium. Reasoning from the analogy of the eruptive fevers, we may suppose that the contagious principle is present in the lesions of the eruptions, that it is carried in the scales which are thrown off during the period of desquamation, that it is contained in the sweat, and that the linen and clothing which have become impregnated with the contagious principle may transport it to a distance. All these opinions are very plausible, and we can only approve fully of the measure of protection based upon them, especially isolation of the affected and the disinfection of the clothing and other objects which have been in immediate contact with the sick, measures which were very generally adopted in the epidemic of 1887.

We must, however, admit that thus far these hypotheses are unsupported by any positive clinical or experimental facts. Attempts made to cause the disease by inoculation of the fluid of the vesicles have proved unsuccessful in the hands of all the experimenters except Parrot. This latter inoculated himself at an autopsy with both the blood of the heart and the fluid from a vesicle. Fifteen hours later he experienced a lively itching on the dorsal surface of the hand and following this there appeared a scarlet patch the size of a silver dollar, which speedily became covered with vesicles resembling in all respects

those seen in the eruption of the prevailing disease. This eruption lasted three days and then gave way to a branny desquamation just as did the eruption of true miliary fever. These inoculation experiments are, however, of only relative importance, for the entrance of the contagium into the body certainly does not take place in the majority of cases through the cutaneous surface.

Contrary to what happens in the case of other contagious diseases, there seem to be absolutely no predisposing conditions of the disease. If we leave aside the very obscure question of the relations of miliary fever to cholera (which disease moreover follows miliary fever much more often than it precedes it), we find that miliary fever seldom attacks one already suffering from another disease, but rather by preference those who are in a robust state of health and in middle life. In many epidemics women have suffered more than men. Most of those who have described epidemics of the disease say that children under ten years of age generally escape. The historians of the epidemic of 1887, however, do not admit this and think that the immunity is often apparent only, and that cases of miliary fever occur in children and even infants, but that they are not recognized, being mistaken usually for measles. In the accounts which we read of many epidemics, it is expressly stated that the appearance of the disease was preceded by an epidemic of measles.

The theory of contagion undoubtedly accounts for many peculiarities observed in the mode of propagation of this disease. It is not at all surprising that in many cases it has not been possible to determine in what way the disease was imported into a special locality, especially if we admit the possibility of mild walking cases, and if we take into account the localities in which many of the epidemics have developed, localities in the country, namely, where medical assistance is not called so promptly as it is in the larger cities.

We may also remark here that miliary fever is not extremely contagious. Alongside of houses in which all or nearly all the inmates have been attacked (14 out of 19 in one farmhouse, in a case cited by Brouardel), there are often many in which only one or two of the inmates have suffered from the disease. In the epidemic observed by Keesbacher the sufferers number 4.8 per cent. of the entire population; in that of Aussee the percentage was 4.4. In the epidemic of Oise the proportions varied in different towns, being 1 in 2 at Ercuis, 1 in 3 at Puyseux, 1 in 6 at Cire, 1 in 9 at Chambly, 1 in 17 at Mello, 1 in 20 at Gouvieux, 1 in 40 at Lys, 1 in 150 at Chantilly, and only 1 in 1,754 at Méru. In 1887 the proportion varied from 1 in 4 to 1 in 20.

The number of sufferers is greater in communes which are situated

nearest to the original centre of the disease, in those where the sanitary conditions are bad, and in those which contain the greatest number of people in poor circumstances or actual paupers. This formula of Rayer expresses very accurately what is known of the conditions of propagation of miliary fever among the individuals in any one locality. It is always in the neighborhood of the original centre of the disease that we find the most numerous and the gravest cases.

In cases in which we cannot trace the origin of the disease to immediate or mediate contagion, we are obliged to assume the propagation of the malady by the air or water, though we are unable to cite any facts in support of this assumption.

In general, as we have remarked above, epidemics of miliary fever arise only in those regions where the disease already exists in endemic form. They begin in localities where isolated cases are from time to time observed, and we are very naturally led to suppose from this that in places where the affection is endemic there exist special conditions which permit the pathogenic agent of the disease to live outside of the human body, most probably in the soil or in the water. Under the influence of certain exciting causes the contagium acquires more active properties, and in this way are to be explained the more or less extensive epidemics occurring from time to time. This hypothesis fits in well with the general feature of the disease, and in this respect miliary fever resembles cholera, malaria, and the plague.

Our knowledge of the conditions common to regions where miliary fever prevails endemically is very slight. However, it seems to be established at least that these regions are damp, more or less marshy, and badly drained. Epidemics appear after seasons of prolonged rains, causing inundations, or of damp and cloudy weather, or, as in the epidemic of Languedoc, after the dredging of the canals. Out of 184 epidemics of miliary fever studied by Hirsch, 83 began in summer, 63 in the spring, 29 in the winter, and 9 in the autumn. When the epidemic occurred in winter it was during an exceptionally mild season, and the occurrence of heavy frosts put an end to the disease, as in the epidemic of Röttingen.

It will be interesting to compare with miliary fever certain epidemics which have been observed after floods, and have been thought to be due to the emanations from the slime left on the surface of the ground by the receding waters. An epidemic of this kind was observed in 1891 in a certain number of places in the district of Coslin in the basin of the Oder River, and was studied by Müller and Schmidtmann. This disease, which was called "Schlammfieber," resembled miliary fever very closely. It had the same rapid onset, sense of fatigue, articular pains, cephalalgia, depression, abdominal

pain, constipation, and sometimes nausea and vomiting. The eruption appeared on the second or third day and usually resembled that of measles. The pharynx and the conjunctiva were quite frequently congested. The sweating does not seem to have been so prominent in this malady as in the classical miliary fever, but Schmidtmann says that it often was present on the fifth day. These cases, in which the etiological influence of the inundation was unquestionable, are worthy of some consideration in the study of the cause of miliary fever.

In the epidemics of Asiatic cholera in 1832, 1849, 1854–55, and in the more recent visitations, the coexistence of miliary fever has frequently been noted. This was in localities where miliary fever is endemic, such as Picardie, Franche Comté, and Provence. The coexistence of these two diseases has puzzled medical men greatly, but it seems to us easily explicable if we will but remember that the exciting causes (heat, moisture, etc.) are equally favorable to the occurrence of miliary fever and to that of cholera.

Prophylaxis.

A comparison of the territories where the disease was endemic in the last century and where it prevails at the present day shows very clearly that miliary fever is diminishing. The improved hygienic conditions and the drying of the soil in consequence of the constantly increasing area of cultivation explain this diminution and lead us to hope for the gradual extinction of the endemic foci of the malady.

Once miliary fever has declared itself in any locality, all our efforts should be to circumscribe it. The means to this end are the same as those employed in the case of contagious diseases in general, namely, isolation of the sick, disinfection of all objects which have come in contact with the patient, and also of the house in which he has been. The history of the epidemic of 1887 seems to have established the efficacy of these measures. Drasche and Weichselbaum also employed them with great advantage in the epidemic of 1892.

The English Sweating Sickness (Suette Anglaise) and Its Relation to Miliary Fever.

From 1485 to 1551 we have records of five successive epidemics of a very grave disease, beginning always in England, in which country it remained limited in all but one of the epidemics.

The affection began with a very violent chill followed by fever. It caused at once an excessive degree of prostration, a painful sense

of weight in the epigastrium, and a feeling of anxiety. The body was bathed with a fetid sweat. All these symptoms occurred in the course of a very short time, and the disease itself had terminated in recovery or death by the expiration of twenty-four hours.

The following is the somewhat less summary account of this disease, which Foucart gives after John Kaye, Bacon, and others: The disease developed suddenly and unexpectedly and announced itself by signs which could not be mistaken for a long period, but which nevertheless varied more or less according to the individual case. Some patients complained of violent pains in the head or in the extremities. Most frequently the affection began with partial sweats on the neck or shoulders, which soon became general; a burning hot vapor spread over the entire body, which soon became literally bathed in sweat. Some felt as if consumed by an internal fire. All complained of an insatiable thirst. They also betrayed an extreme agitation, anxiety, uneasiness, oppression, and an excessive prostration. In some cases there was great loquacity followed by an invincible tendency to sleep; the scene was terminated by a soporous delirium, which led the ignorant public to believe that it was the sleep itself which was the cause of death, instead of being merely one of the symptoms of a fatal disease. In some patients the gastric functions were arrested and incoercible vomiting occurred whenever the least thing was taken into the stomach. Among all there were extremely painful palpitations and precordial anxiety. The pulse was small and frequent and the respirations were accelerated, short, and labored. Sometimes the sweating stopped and the extremities became cold, but this was only temporary and it returned as soon as the members became warm again. The urine was either normal or fetid. All these symptoms lasted usually for eighteen to twenty-four hours, sometimes less, and at the end of this time either the patient recovered or death occurred. After twenty-four hours the danger was past, but the disease left behind itself a weakness of very long duration, and also palpitations which persisted several years after recovery or sometimes for the rest of life.

The duration of the disease varied in different epidemics. In some cases it lasted three or four hours only, in other cases the progress was less rapid and the affection was of less gravity.

The first invasion of this malady was in the month of August, 1485, and occurred on the west coast of England. London was invaded at the beginning of September, and the ravages caused there by the sweating sickness were very considerable among the leading citizens, six aldermen and the Lord Mayor succumbing in the course of one week.

The disease appeared a second time during the summer of 1506 and terminated in the autumn of the same year. This second epidemic was attended with a much lighter mortality than the first. Details concerning its progress are wanting, and we only know that London was invaded. The sweating sickness appeared a third time in July, 1517, and this time the mortality was very great. The disease prevailed all over England and even crossed the Channel and attacked Calais, although here all the native population escaped, only Englishmen being attacked.

Eleven years had separated the third epidemic from the second, and the same interval elapsed between the third and fourth epidemics. This time the disease was discovered in London at the end of May and caused great ravages in England. The pest on this occasion did not remain confined to England but appeared the following year in Germany, where the first cases were reported in Hamburg on July 25th, and in Lübeck on the 29th of the same month, and other places in the country were successively invaded, Zwickau in the beginning of August, Stettin in the first part of September, and Dantzig, Augsburg, Cologne, Strasburg, and Frankfort at the same time. The Low Countries were invaded the latter part of September, and Denmark, Sweden, Norway, Lithuania, and Poland followed in turn. Everywhere the disease appeared with the same characters as to gravity and extent of diffusion. Everywhere the duration of the epidemic was short, from four to five weeks, and by the end of the year 1529 it had disappeared entirely.

The sweating sickness appeared for the fifth time in 1551 at Shrewsbury on the Severn. It travelled from the west to the east, but more slowly than in the previous epidemics, for it did not reach London until the 9th of July. It extended all over England, however, and died out on September 30th, after having claimed numerous victims in all classes of society. This was the last epidemic of the sweating sickness in England, and the affection has never returned from that day to this.

In two of these epidemics the march of the disease was quite clearly followed. Both times England was traversed from west to east, the first important city invaded in 1485 as well as in 1551 having been Shrewsbury on the banks of the Severn. The disease seems to have been a contagious affection, for we see it following Henry VII. and his army into London after the battle of Bosworth Field.

The epidemic of Hamburg in 1529 was attributed by contemporary writers to an importation from England. However this may have been, the fact is that the first persons attacked were members of

the crew of a vessel arrived from an English port. During the epidemics of 1517 and 1528 Henry VIII. and his court escaped infection by means of strict isolation.

The disease always attacked vigorous subjects in the prime of life and preferably those who were great eaters and drinkers. Caïus even alleges this latter as the reason why the English were the only persons attacked in Calais, Antwerp, and several cities in Brabant in 1551, the natives of these places escaping wholly. The true explanation of this predilection for the English was undoubtedly that those attacked had just come from across the Channel and had been infected in their own country before departing, or else that the contagion was conveyed to them in articles brought from England and which had been in contact with the sick.

The English sweating sickness began in the spring or summer. The historians of the epidemic of 1551 state expressly that the weather that year was hot and damp, and they speak of miasmatic exhalations arising from the river Severn.

The facts which we have just recounted, namely, the influence of contagion, the happy effects of isolation as a prophylactic measure, the predilection of the disease for vigorous subjects, its appearance in the spring and summer and in damp localities, all point to the probable identity of the English sweating sickness and miliary fever. Authors who, like Rayer, Foucart, Guérin, Hirsch, Colin, and myself, believe in the identity of these two affections, base their opinion chiefly on the clinical characters. The profuse sweat was always the essential factor in the English epidemics, and with this sweat were associated the nervous symptoms, a painful weight in the epigastrium, a sensation as of strangulation, depression, palpitation of the heart, coldness of the extremities, great anxiety, somnolence, and sometimes delirium. These very nervous phenomena are found in the miliary fever of the present day.

Those who oppose the view of the identity of the two affections allege the extreme diffusion of the English disease, the rapidity of its progress, the incomparably greater gravity, and the absence of eruption. All the writers who described the English sweating sickness dwelt especially upon the absence of eruption as a feature differentiating the disease from the two other great epidemic diseases of the time, to wit, the plague and typhus fever. But the eruption in miliary fever is a late phenomenon, appearing only on the third or fourth day, and it would therefore naturally not have been observed in cases which ran their course so rapidly as did those in the English epidemics of sweating sickness. We may suppose that the authors, confining themselves especially to a description of the fatal cases,

overlooked the eruption which occurred only in the more prolonged and atypical cases. But Tyengius, who studied the epidemic in Holland in 1529, refers to the occurrence of a vesicular eruption on the extremities towards the end of the disease.

The gravity of the English sweating sickness does not appear to me to be a sufficiently distinctive characteristic to separate it absolutely from miliary fever. It may be explained in part by the very unfortunate therapeutic measures to which resort was had in those times. All writers describing recent outbreaks of miliary fever are agreed in regard to the injurious effects of covering the patients with a heap of bedclothes, which is done in domestic practice by the peasants with the idea of increasing the sweating, and we know that this was the universal practice in the Middle Ages. Again, although in the great majority of modern epidemics of miliary fever the disease is of benign type, it is not always so. We have already seen that in the Aussee epidemic in 1893, the deaths were over one in four, and we cannot call an affection which may be attended with such a mortality an insignificant one. These fatal cases also sometimes progress with great rapidity. Parrot speaks of a fatal result being reached in from three to six hours, and we have seen in the section on prognosis that these are not isolated instances.

We will admit that the English epidemics spread with much greater rapidity and over a wider extent of territory than have any of the epidemics of miliary fever, but this is only a question of degree, for the extent and rapidity of diffusion have been very noticeable in some of the outbreaks of the latter disease. The celebrated medical historian, Hecker, who moreover was not an upholder of the identity of the two affections we are now considering, has told us of the occurrence of a grave disease having the same characteristics as the English sweat, but which was of limited exent, at a period much more nearly approaching our own times. The little German city of Röttingen on the borders of the Tauber in Franconia was visited on November 25th, 1802, with an absolutely new disease, of which the following were the main characteristics: The disease attacked young and vigorous subjects, beginning suddenly with a feeling of inexplicable anxiety; the heart beat violently against the ribs, a lancinating pain was felt at the base of the neck, radiating thence to the chest, which was accompanied by a trembling of all the extremities. The body was covered with a profuse acid and fetid sweat. Most of the sufferers succumbed within a period of twenty-four hours, but some began to improve on the second day although the sweating continued up to the fifth day. A certain number suffered a relapse. There does not appear to have been any eruption, or at least Sinner, who

described the disease, says that what eruption there was in certain cases was caused by the medicines exhibited.

The malady had had many victims up to the time that Sinner, called from Würzburg, succeeded in inducing the inhabitants to abandon their method of forced sweating to which till then they had had recourse, and which had been as unhappy in its results as in the English epidemics in the sixteenth century. There were no new cases after December 5th, on which day the weather, which had been unseasonably mild, became cold.

Mead furnishes us with a final argument in favor of the identity of the sweating sickness and miliary fever. He tells us that in 1713 the English soldiers in Dunkirk contracted a disease which they carried with them to England in the month of September. This disease, he says, had the same features as the sweating sickness of the Middle Ages; and furthermore, he asserts, the first epidemic in 1485 had been imported from France. It was in this country that the Duke of Richmond had recruited the army which was to put him in possession of the throne of England. He embarked at Havre the end of July and landed on August 1st. The first cases of the disease were among his troops, and the sweating sickness followed his triumphal progress to London.

We believe, therefore, resting our argument on the facts above related, that miliary fever is the same disease as the English sweating sickness of the Middle Ages, the latter being distinguished only by its wider extent and its greater gravity, and that consequently we ought to study with even more care than hitherto this curious affection and stretch every endeavor to cause its entire disappearance. The more and more restricted domain of its endemicity and its disappearance from England for a century and a half, where it formerly prevailed with such murderous effect, give us reason to hope that this happy result may be expected without too tedious a delay.

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MALTA FEVER.

BY

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BRITISH ARMY.

MALTA FEVER.

Synonyms.—Mediterranean fever (various writers); gastric remittent and bilious remittent fever (Marston, 1861); Mediterranean gastric remittent fever (Chartres, 1865; Boileau, 1866); la febbre gastrobiliosa (Gulia, 1871); fæco-malarial fever (Donaldson, 1876); intermittent typhoid (Borrelli, 1877); adeno-typhoid (Cantani); febris complicata (Veale, 1879); febris sudoralis (Tomasselli, 1880); pythogenic septicæmia (Moffet, 1889); undulant fever (Hughes, 1896); rock fever, Neapolitan fever, etc.

Definition.—A disease of long duration, characterized clinically by fever, profuse perspiration, constipation, frequent relapses, often accompanied or followed by pains of a rheumatic or neuralgic character, sometimes swelling of joints or orchitis; anatomically by enlargement and softening of the spleen, congestion of the various organs, no enlargement or ulceration of Peyer's or other intestinal glands, and the constant occurrence in various tissues of a species of micro-organism, the micrococcus melitensis.

Geographical Distribution.

This fever, which does not appear to occur in England, has a wide distribution along the shores and among the islands of the Mediterranean. As it has probably been more thoroughly studied in Malta than in any other locality, a short description of this island will not be superfluous. Malta is a small island, being only some seventeen miles long and nine miles broad. It is built up altogether of sedimentary rocks which have been divided by geologists into upper and lower limestones, and various intermediate beds of sandstone. These beds of sandstone are mostly formed of a very porous stone, and are traversed by innumerable fissures. Between the sandstones and the upper limestone there is a bed of marl which plays an important function in regard to the water-supply of Malta. The eastern half of the island, and by far the most populous part, has been denuded of the upper limestone and marl, so that almost all the cities and villages of Malta are built on a porous sandstone. The rocks are usually regarded by geologists as belonging to the Pliocene forma-

tion. A microscopical examination shows that the upper and lower limestones are composed of corallines, calcareous algæ, and large foraminifera; whereas the so-called sandstones are made up of pelagic foraminifera resembling in many respects, and to a very large extent, deep sea deposits.

Malta is one of the most densely populated places in the world. According to Dr. Cousin, the able author of the last British census, the proportion of the population, exclusive of Her Majesty's troops, is 1,443.12 to the square mile. Nearly one-half of this population (sixty-seven thousand) is concentrated, as might be expected, in the vicinity of the magnificent harbor, called the Grand Harbor, the shipping of which affords employment to thousands of the poorer inhabitants of the neighboring cities and villages.

Valletta, the capital of Malta, is a handsomely built city, and to a stranger passing through appears to be very clean; but the houses are badly constructed, being lofty and built round narrow, well-like courts, down which little sunlight and pure air can struggle. The area of Valetta is only one-third of a square mile, and into this narrow space are crowded some thirty thousand persons.

The three fortified cities built on the other side of the Grand Harbor may be described together, and in a few words. The buildings are similar in structure to those in Valletta, but are inhabited by a poorer class of people. Senglia and Vittoriosa are both built upon high ridges with steep sides. Cospicua of the three is the most huddled together, overcrowded, and has the poorest class of population.

Let us now direct our attention for a few minutes to the country villages or casals of Malta. To begin with the unit, or building inhabited by one family. The plan is very simple, and was probably devised for motives of safety, when the island was apt to be overrun by any piratical crew. There is first built a square enclosure of the surrounding sandstone. The size of this enclosure, we shall say, is twenty feet square and twelve or fourteen feet high. In one of the sides a doorway is built for the purpose of gaining access to the interior. Against the inner walls are built various sized cabins with flat roofs. These cabins have no windows, but depend altogether for light and ventilation on a doorway. When these cabins are ranged against the walls, the original building area of, say, fifty square yards is reduced to some ten or twelve. This remains roofless, and is the courtyard. These enclosures are closely packed together in double rows, and the lane running between them is, in many I have examined, not more than six or seven feet wide.

In the small courtyard of one of these village houses all the oper-

ations of life are carried on, such as cooking, eating, washing, etc. In one corner may be seen an uncovered and exceedingly primitive privy. In another the opening of the underground tank for drinking-water. Near the door of the living-room there is often scooped out a hole or cellar into which is thrown all the refuse resulting from cooking operations. One of the cabin-like structures is used as a manure-room, wherein is stored as much filth and rubbish as possible, to be sold at intervals to the neighboring farmers to spread over the fields. In others are found rabbits, poultry, and possibly a goat or pig. In a pent-up enclosure of this kind, reeking with all sorts of smells and swarming with flies and vermin, there usually lives a man, his wife, and family of several children. These miniature courtyards are often very picturesque, with flowering plants scattered about, or a bright green vine trailing its branches irregularly over a corner of the enclosure, or partly roofing it by being trained along rude trellis-work. These plants, as might be expected, grow luxuriantly in the rich atmosphere of the courtyards, where they are protected from every breath of air.

Having thus dwelt briefly on the form of dwelling and population of the cities and villages of Malta, let us turn to an important point, namely, their water-supply.

Valletta and the three cities are supplied principally by water collected from the springs in the upper limestone hills, some eight miles to the southwest. In the paragraph on the geological formation of Malta, it will be remembered that lying under the upper limestone there is a bed of marl. Headings are driven for great distances at the junction of the limestone and marl, and the water, percolating through the very porous limestone, is caught on the marl, and finds its way in small streams along these headings to be collected and conveyed to Valletta and the three cities by iron pipes under pressure.

The villages have the worst water-supply. The only source is the water collected from the roofs, courtyards, and lanes. In fact, in many of these enclosed dwellings which I have examined, the rain is led by pipes from the roofs of the cabins to the courtyard, across which it streams and gains access to the tank through an opening in the neck on a slightly lower level than the courtyard. From the description given above of the general filthy condition of these courtyards—swarming with children, dogs, and poultry—some idea of the contaminated condition of the water in these tanks may be formed.

Let us now turn our attention to the removal of sewage in Malta.

As in treating of the water-supply, I shall begin with Valletta and the three cities.

For the removal of sewage from these cities a complete and costly

system of drainage by water-carriage has been carried out during the last few years. In the year 1865 the drainage was effected by means of narrow channels cut in the porous sandstone, which conveyed, or failed to convey, the sewage into the harbors. The new main drain conveys the sewage by a circuitous route several miles in length, and pours it into the sea at some distance from the mouth of the Grand Harbor. In a report on this system of drainage, it appears that the street sewers were found on inspection to be practically clean, that the gradients were sufficient to give a rapid flow, and the flushing apparatus worked efficiently. But the condition of the house drains was less satisfactory. In almost every instance there was strong evidence of stagnation within the house drains. The members of the sub-committee satisfied themselves of this, in several instances, by pouring water down the drain and observing the putrid sewage which came out with the first flow. The sewage flow seen in the street sewers was black and putrid even close to the heads, giving further evidence of stagnation in the house drains.

This defective action of the house drainage is attributed to defective construction, principally as regards workmanship and improper usage on the part of the occupiers.

From this it would appear that although a great advance has been made in the drainage of the fortified cities, there still remains much to be done.

In the villages there are two methods of getting rid of the sewage. One is by pouring it into cesspools in the vicinity of the houses; the other, by throwing it into one of the rooms of the dwelling, which receives the name of manure-room. In the central set of villages the sewage is as a rule got rid of by the cesspool system. By law these houses should be drained into separate water-tight cesspools in the street. But this would entail the trouble of frequent emptying, so the builder, taking advantage of the numerous fissures in the porous sandstone, takes care that the cesspool will communicate with one of them. Mr. Osbert Chadwick, C. E., in a memorandum on drainage, states that these cesspools may be cemented to the satisfaction of the sanitary inspector, but as soon as he is gone a few blows of a pick-axe suffice to make a leak. Many of these cesspools have never been emptied since they were made, the contents slowly leaking into the porous rock. As may well be imagined, this is a fruitful source of contamination to neighboring wells. But the manure-room is the most transcendant abomination. This obtains, as was pointed out in a previous paragraph, in most of the poorer villages, where manure is valuable for use in the neighboring fields. In this room, close to the living rooms and pent up by the enclosing walls, all the filth and

refuse of the family and animals is stored. This hoard is increased by the daily addition of dung scraped up from the streets or roads by the younger members of the family.

From what has been noted, it is evident that the sanitary condition of Malta, as regards drinking-water and drainage, is mostly in a very barbarous condition, but as regards the most densely peopled part of the island, viz., Valletta and the three cities, a very great deal has been done within the last few years. These cities, from being among the worst drained and worst watered of Mediterranean cities, are now among the best. But in regard to overcrowding, the condition is becoming daily worse. In the report of the cholera commission it is stated "that the fortified cities, and even some parts of the villages of Malta, are overcrowded to an extent that is dangerous to public health." Many blocks of houses exist so closely packed together that it is impossible to secure the proper amount of light and air. The general arrangements of the existing villages, as we have seen, is highly insanitary. From the narrow, tortuous streets lanes branch off which are even narrower and more irregular. These are the only means of access to the densely built-over quarters, and they often terminate in blind ends. There is, therefore, an inadequate supply both of light and of air.

From the foregoing description and from the fact that for centuries most insanitary conditions have prevailed, it need not be wondered at if such semi-Oriental cities have proved a fit nursery for the rearing of a new form of infectious fever.

That the fever, as it occurs in Malta, is identical with the so-called rock fever of Gibraltar, there can be no doubt, ample opportunity having been afforded at the Royal Victoria Hospital, Netley, of comparing cases from both places. I have also had the opportunity of studying in the Naval Hospital, Malta, cases of fever contracted in many of the Mediterranean harbors visited by the British fleet, and have completely convinced myself of their identity with the disease under consideration.

In Italy it has been described as occurring at Naples and other towns along the coast. Cagliari in Sardinia, Catania in Sicily, Candia in Crete, Constantinople, Smyrna, Tunis, and Algiers may also be mentioned as towns in which this fever appears to be endemic.

On further investigation, and when the characters and specificity of this form of fever are better recognized, I have no doubt the area of its distribution will be much extended, and many cases at present confounded with typhoid and malarial fevers will be found to be identical with it.

In this connection Professor Wright and Surgeon-Captain Smith

have lately published some interesting observations "On the Application of the Serum Test to the Differential Diagnosis of Typhoid and Malta Fever." They consider "that this test discloses the fact that Malta fever is, as Bruce and others have long surmised, a disease which is not by any means confined to the Mediterranean basin." They have what they take to be definite evidence of its existence in three stations in Northern India and also probable evidence of its existence in Hong-Kong.

Etiology.

Bacteriology.

The microorganism of Malta fever was first discovered by me in Malta in 1887, and since then its constant occurrence in the organs of fatal cases of this fever has been verified in the same island by various observers. During the last ten years the evidence accumulated goes to prove that this organism is undoubtedly the *causa vera* of Malta fever.

It is found in every fatal case. Pure cultures injected under the skin of monkeys give rise to all the phenomena of the fever. It shows the characteristic clumping phenomenon on the addition of serum from cases of Malta fever; and, lastly, one positive case of accidental inoculation by a pure culture has occurred in man.

In regard to its morphology, the micrococcus may be described as round or slightly oval in form, and measures in dried preparations about 0.3 μ in diameter. Viewed in a drop of water unstained, the microbes are seen as bright points in active molecular movement, the great majority of them single, a few in pairs, but never in chains. Like most micrococci they possess no power of spontaneous movement. They can be readily stained in a watery solution of gentian violet, but Gram's method is not applicable, as they become decolorized in the process. When planted in nutrient peptonized broth and kept at 37° C., no change can be seen for the first few days, but after some time the fluid becomes decidedly cloudy without any formation of pellicle on the surface.

The best medium for the cultivation of this species is ordinary one and one-half per cent. peptonized agar-agar beef jelly. The inoculation into the agar-agar tubes may be made either as a stab culture, or by spreading the material over the surface of the agar-agar, which has been solidified in a sloping position, so as to give a large surface. In the stab cultivations made from the spleen of a

fatal case or from a previous culture, no change takes place in the appearance of the jelly for several days. At length the growth appears as minute pearly white spots scattered round the point of puncture, and minute round white colonies are also seen along the course of the needle track. After some weeks the colonies on the surface grow larger and join to form a rosette-shaped colony, while the needle track becomes strongly marked, solid looking, and yellowish-brown in color, with serrated edges. After the lapse of some months the growth remains restricted in area and its color deepens to buff.

When growing on the sloping surface of agar-agar and examined by transmitted light, the appearance of the colonies is somewhat different. At the end of nine or ten days, if kept at 37° C., some of the colonies have a diameter of 2 to 3 mm. They are round in shape, with an even contour, slightly raised above the surface of the agar-agar, and smooth and shining in appearance. On holding up the tube and examining such colonies by transmitted light, the centre of each is seen to be yellowish in color, while the periphery appears bluish-white. On looking at the same colonies by reflected light, no appearance of yellow can be seen; they then simply appear to be milky-white in color. The separate colonies on the surface of the agar-agar do not extend indefinitely, and after a couple of months are found to be no larger than hemp seeds.

The time which elapses before the growth of this micrococcus can be seen by the naked eye is fairly constant. Kept at a temperature of 25° C., this period may be stated to be seven days; at 37° C., about half that time.

When stab cultivations are made into ten-per-cent. nutrient gelatin, and kept at 22° C., little or no growth takes place; after a month the needle track has become slightly developed, and on the surface can sometimes be seen a minute, smooth, white growth, not larger than a pin's head. No liquefaction of the gelatin takes place.

Gelatin plate cultivations of this species are not practical, on account of the extreme slowness of growth at the temperature at which this medium remains solid.

Planted on boiled potato and kept at blood temperature, no apparent growth takes place.

The temperature charts which follow represent a few fatal cases of Malta fever, from which the micrococcus melitensis was cultivated. This micrococcus up to the present has been obtained from some thirty cases of fever.

CASE I.—H. D——, aged 24. Autopsy ten minutes after death. No enlargement or ulceration of the lymph follicles of the intestine.

The chart (Fig. 15) represents the course of the disease.

CASE II.—B. D——, aged 28. Autopsy ten minutes after death. No ulceration or enlargement of the lymph follicles of the intestine.

The chart (Fig. 16) represents the course of the disease.

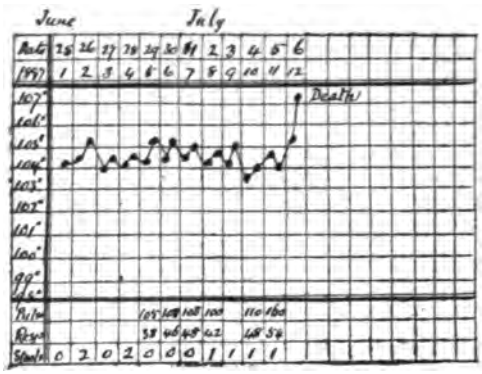

FIG. 15.

CASE III.—J. C——, aged 22. Autopsy ten minutes after death. No enlargement or ulceration of the lymph follicles of the intestine.

The chart (Fig. 17) represents the course of the disease.

CASE IV.—T. G——, aged 23. Autopsy ten minutes after death. No enlargement or ulceration of the lymph follicles of the intestine.

The chart (Fig. 18) represents the course of the disease.

From these cases and many others in every instance pure cultures of the micrococcus melitensis were obtained. As a rule, the inoculations were made from the spleen, but sometimes also from the liver and kidneys.

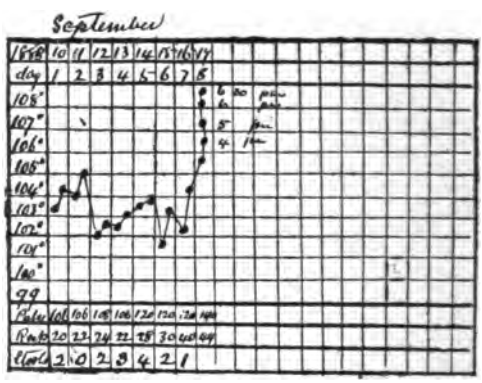

FIG. 16.

The microbe of Malta fever seems to be almost altogether absent from the circulating blood, as I have proved by numerous experiments. Surgeon-Captain Hughes, however, states that he has been able to cultivate it from the blood of the heart of a monkey dead of the disease.

Besides cultivating this species from the fresh organs after death, I have also succeeded in some cases in obtaining it by splenic puncture during life, so that the constant occurrence in cases of Malta fever of a definite species of micrococcus may be held as proved.

The effect of the inoculation of a small quantity of a pure culture

of the micrococcus of Malta fever under the skin of mice, guinea-pigs, and rabbits is altogether negative. With monkeys, however, the result is more successful, as the following experiments will show.

Experiment I.—Monkey, ♂, sp. Bonnet. The temperature of this monkey for a fortnight before inoculation ranged between 99° and 100° F. He ate well, was very active, and to all appearance healthy. The material used for inoculation was a portion of a colony removed from an agar-agar tube, and rubbed up with a small quantity of sterilized water. This suspension was injected into the skin of the monkey's forearm under stringent antiseptic precautions. The tube from which the material was taken was a cultivation taken from Case I., and had been growing outside the body for a month.

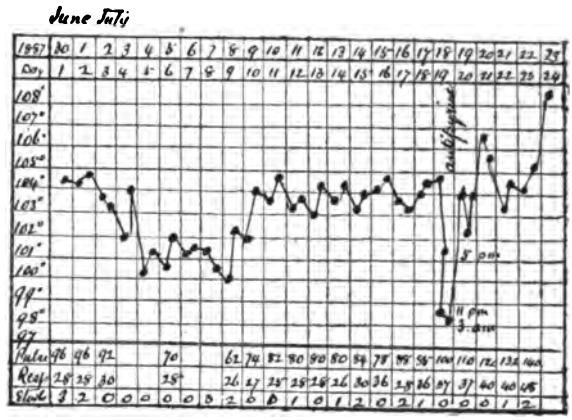

FIG. 17.

The chart (Fig. 19) shows the course of the disease.

On post-mortem examination the lungs showed no signs of tuberculosis, the liver was congested, the spleen enormously enlarged, and the mucous membrane of the intestines free from ulceration. Immediately after death six tubes of agar were inoculated from the spleen and two from the liver. In all the spleen and in one of the liver tubes the growth characteristic of the micrococcus of Malta fever appeared after the usual time. In the second liver tube no growth of any kind took place.

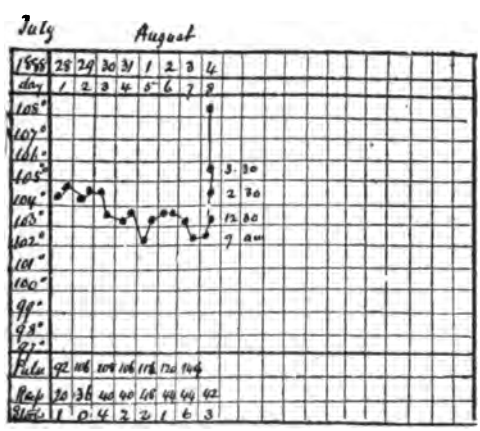

FIG. 18.

Experiment II.—Monkey, ♂, sp. Bonnet. Inoculated in the same manner as in the last experiment. This monkey's temperature also

ran high, and he died after thirteen days' illness. Inoculations from the organs into agar tubes showed the first appearance of pure cultures after four days.

Surgeon-Captain Hughes has also been successful in transmitting Malta fever to monkeys in several cases, notes of one of which he has kindly sent to me, and which I shall now give.

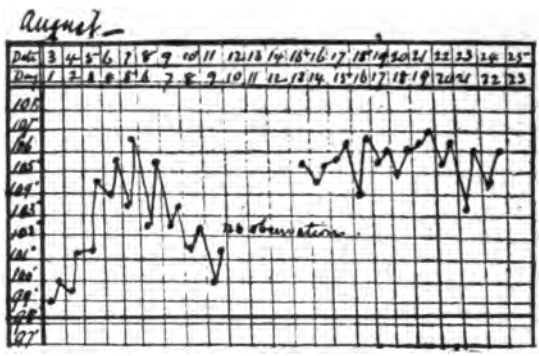

FIG. 19.

Experiment III.—Monkey, ♂, sp. Bonnet. This monkey was under observation for two months, during which time his appetite was good and his temperature normal.

He was inoculated in the forearm by injecting 1 c.c. of sterilized broth in which had been rubbed up a small quantity of growth from a twenty-four-day old agar tube. The temperature went steadily up, reaching 106° F. on the fifteenth day of illness. For the first ten days the monkey was lively and continued to eat his food, but after this time he began to lie about and refuse his food. Death occurred sixteen days after inoculation.

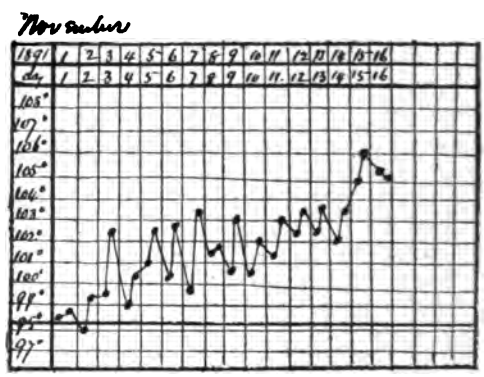

FIG. 20.

The chart (Fig. 20) represents the course of the disease.

Post-mortem Examination.—The body was fairly well nourished. Heart apparently normal. Lungs contained some seropurulent exudation in the bronchi, otherwise they appeared healthy. Liver enlarged and congested. Intestines showed some congestion at the ileocæcal valve, otherwise normal.. Spleen much enlarged and congested. Inoculations into agar tubes from the spleen and liver showed the growth of the micrococcus after the usual time.

In all seven monkeys have been inoculated with pure cultures of

the micrococcus melitensis, four by Surgeon-Captain Hughes and three by myself. Of these, four died with all the symptoms of the fever as observed in man, and from their organs the same microbe was recovered in a state of pure culture. The other three monkeys recovered after more or less severe illness, in two cases lasting two and a half and three months respectively, and according to Surgeon-Captain Hughes' statement showing in a remarkable manner the typical intermittent waves of pyrexia as observed in man.

From the above considerations sufficient evidence has in my opinion been brought forward to show that the micrococcus above described is the cause of Malta fever, and is the strongest evidence yet adduced to show that this disease is a specific fever, quite distinct from typhoid or malaria.

In regard to the important question as to how this microorganism gains access to the human subject, whether by the air, in the drinking-water, or in the food, absolutely nothing is known up to the present, and on account of the high temperature required for its growth, the length of time which elapses before the colonies appear, and the absence of any well-marked morphological or cultural characteristics, the search for it outside the body will be very difficult, if not fruitless.

Age and Sex.

As the great majority of the English soldiers stationed in Malta are young men, statistics in regard to age are of little value. I may, however, state that sex seems to have little or no influence, and that youth, as is natural, is a predisposing factor. If the disease occurs among the very young it is difficult to be certain of the diagnosis, and it is probably often overlooked. The opinion of the native practitioners is that the greatest number of cases occurs between the ages of six to thirty, less frequently from two to six and from thirty to fifty, and very rarely above fifty. This may be true for the native population who live all their lives in the infective area, without being true for strangers arriving there. In my opinion, given a susceptible constitution, any age is liable to this fever, but that for a variety of reasons the liability is exaggerated in those under thirty-five.

Mode of Prevalence.

In Malta this fever is endemic and never altogether absent; but now and then the cases become so numerous as to constitute epidemics. Some of these outbreaks have been attributed to the general immaturity and want of acclimatization of the men of some regiments

landing from England during the unhealthy season; in others, the cause has been assigned to the insanitary condition of certain of the barracks. Be this as it may, it is also certain that Malta fever attacks officers and their families living in large, well-ventilated houses, probably in as large a proportion as it does soldiers in the more crowded barrack rooms.

Months and Seasons.

In regard to the months and seasons in which Malta fever is most prevalent, the following chart (Fig. 21) represents the number of

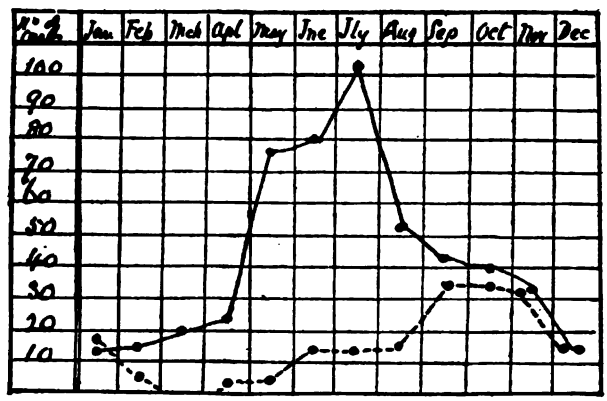

Fig. 21.

cases admitted during each month for eleven years from a garrison of some three thousand soldiers. For the sake of comparison, the admissions for enteric fever during the same period are represented by a dotted line. From these it will be seen that Malta fever is a disease of summer, most cases occurring in July, whereas enteric fever is a disease of autumn and early winter.

Mode of Dissemination.

Malta fever, so far as I know, is never transmitted directly from person to person. In the hospitals in Malta, although cases are to be found all the year round scattered through the various wards, there is no evidence that it has been communicated to any of the other patients in a single instance. As I have before stated, it is impossible with our present knowledge to say whether the poison gains entrance to the organism by the respiratory or alimentary organs. The tendency is to believe that it floats in the air, especially

in the neighborhood of foul drains or other insanitary conditions, and so reaches the body by being breathed in. A bad smell *per se* cannot give rise to a specific fever, although it may lower the general health and so predispose to disease.

Since this fever is caused by a definite vegetable organism, it is difficult to picture such a particle rising into the air from fluid or solid substances in which it may be supposed to find a suitable soil for growth. On this account it is probable that Malta fever, like typhoid, is chiefly carried by means of the drinking-water or other fluid or solid foods to which the contagium has gained access.

Pathological Anatomy.

As would be expected, the changes found are those due to high temperature and some irritating property in the blood. On making a section through a Peyer's patch and examining it under a low power, the serous, muscular, submucous, and mucous layers are found to be unthickened and almost normal in appearance. The epithelial layer is continuous over the surface of the gland. Under a high power, morbid changes are found restricted to the mucous and submucous layers, and consist in a slight proliferation of the cellular elements. On examining the large endothelioid plates of the glandular tissue they are seen to be somewhat swollen and proliferating, and there is a slight proliferation of the adenoid tissue. The mesenteric glands are slightly enlarging; there is proliferation of the cellular elements of the lymphoid tissue; the reticulum is very delicate, and appears in places to be almost obliterated by the increase in the number of the cells; there is some proliferation of the endothelioid plates and they are in a condition of cloudy swelling. The spleen weighs on an average eighteen ounces, and is soft and diffluent; the Malpighian bodies are enlarged from an apparent increase in the number of the round lymphoid cells; the endothelioid plates of the marginal sinuses are proliferating and swollen; a condition of intense congestion is seen in the section, the sinuses being enormously distended with blood; there is a marked exudation of small round cells along the lines of most of the venules. The liver is congested, the cells are in a condition of cloudy swelling, and there is an infiltration of small round cells in the interlobular fissures. The kidneys are also congested, and in a condition of glomerular nephritis.

Symptoms.

Incubation.

It is impossible to state definitely how long the period of incubation is, but it ranges probably from a few days to twenty or thirty. In an epidemic which broke out in one of the barracks in Malta, the first cases occurred six days after the arrival of the regiment. Again instances are on record in which the disease has broken out in individuals on their arrival in England, fourteen and seventeen days after leaving Malta. But the important point to note in this regard is, that there is no evidence to show that this period of latency is much longer than above stated, so that individuals who remain free from the fever for say two months after leaving the infective area may be considered safe from attack.

Early Symptoms.

A patient suffering from Malta fever, on being admitted into hospital, usually states that he has been feeling out of sorts for a week or two; his appetite has been fickle; vague feelings of discomfort, as shivering, sickness, headache, and pains in his bones, have often been present, and to escape his now irksome and wearisome duties he has sought admission to hospital. For the first week or ten days he often suffers from sleeplessness and headache, which may vary from the mildest form to the most intense, very often frontal, and more rarely shooting from the occiput through the eyes. In these severe cases the face is usually congested, the ears are ringing, and epistaxis may occur. The tongue is generally covered with a thin, yellowish-white fur; it is large and flabby, the edges and tips are red, and it is usually marked laterally by the teeth. Congestion of the pharynx is often present. The appetite is absent; there are nausea, sometimes leading to vomiting, and a feeling of weight and tenderness in the epigastric region. The bowels are constipated, as a rule, but errors in diet or excessive use of medicine may bring on attacks of diarrhœa. The stools are sometimes streaked with blood. The spleen and liver are enlarged and both may be tender on pressure. Tympanites is uncommon, but may occur, as also may gurgling in the iliac fossa. During this time almost invariably a slight cough, with scanty expectoration, is developed; and on examination the breathing at the bases is found to be unsatisfactory, harsh, and creaking in character, with now and then a moist crepitation. Morning after morning the patient is found to be bathed in a most profuse perspi-

ration, and a more or less abundant crop of sudamina is developed. He may have had a little delirium at night during this time; but this is rare, and is so slight as scarcely to call for remark. Unless there is severe headache or pain in the lumbar region, the patient during the first week or two usually professes that he suffers very little. At the end of this period the headache and acute symptoms usually disappear, and the long and monotonous period of the fever begins—a period which seems interminable alike to medical officer and patient. The patient's aspect is natural, but listless; his tongue is clean; he has a wish for solid food, which must often be denied, and his bowels require the stimulus of an aperient or enema for evacuation.

Later Symptoms.

The profuse perspiration still continues, and day after day the patient becomes weaker and loses weight until he has scarcely power to stagger a few yards. His red blood corpuscles diminish in number, and his complexion changes from pale to sallow, and from sallow to a dull clay color. During this period his temperature often ranges high, but he professes to be quite unconscious of any change in his condition. He sleeps moderately well, has no delirium or restlessness, is uncomplaining, and takes without any ill effect a large supply of fluid food and stimulants. The only variety in his condition is afforded by a rheumatic affection of the joints; one day it is a knee which is red and swollen, and intensely painful on being touched; a few days after it is a swollen and deformed wrist which he holds up for commiseration. Sometimes almost every joint in his body is attacked in this manner, or he may have intercostal neuralgia, sciatica, or an inflamed and swollen testicle. In this way many weeks are long drawn out; but at last his temperature fairly comes down to the normal, and he begins very slowly to improve, his blood corpuscles gradually regain their normal number, his weight increases, and his strength is slowly restored. This is a clinical picture of an ordinary well-marked case; but the fever may occur in such a mild degree that the rise in temperature is the only morbid phenomenon. On the other hand it may be so severe as to be absolutely indistinguishable from the most rapidly fatal case of typhoid.

Principal Symptoms in Detail.

Physiognomy.

The expression of the face, in the great majority of cases, may be summed up as being dull, listless, apathetic, anæmic. During the first onset, when there is severe headache, the face and exposed

mucous surfaces are often congested, and the patient has an excited, restless look; but this soon disappears, and is replaced by lethargy. In long and severe cases, the face may become of a dull-gray color; and as the patient in this condition has left all hope behind, his expression is naturally despondent in the extreme.

Alimentary System.

The tongue is at first more or less thickly covered with gray or yellowish-gray fur; afterwards, as a rule, it is large, flabby, indented by the teeth, and covered with a thin, translucent fur, except the tip and edges, which are red. In about ten per cent. of the cases, the tongue becomes dry and brown for some days during the progress of the disease, and in a few the dorsum becomes fissured, with a little blood oozing from the fissures. In many cases the gums, as the disease advances, are found to be soft and spongy, and in some cases bleeding from the gums is noted. The fauces are usually somewhat congested. Vomiting, except in severe attacks of this fever, is not a marked symptom; but when this occurs the vomited matter is frequently streaked with blood. Nausea is much more commonly complained of than vomiting; and as is natural, anorexia is almost invariably present at the beginning of the fever. Constipation is one of the marked features of this disease. In 65 cases in which the condition of the bowels was carefully noted, in 48 there was constipation throughout and in 17 only did diarrhœa occur at any time during the illness. Murchison states that he noted constipation in 4 and diarrhœa in 93 out of 100 cases of enteric fever. It is evident in Malta fever that constipation is the rule and diarrhœa the exception. The reason of this is not far to seek. In post-mortem examinations of cases of enteric fever, ulceration and an inflamed condition of the lower end of the small intestine are found, which must necessarily have tended to diarrhœa; while in Malta fever no such ulceration or inflammation occurs. Tympanites is rare, and ascites still more so. The liver is usually slightly enlarged, sometimes painful on pressure, and slight jaundice may be noted occasionally.

Respiratory System.

Epistaxis occurs in about one-sixth of the cases. Cough at one time or another almost always occurs, and is marked in one-half of the cases; in these the expectoration is sometimes profuse, and is often streaked with blood. Even when there is no cough the breathing is found to be unsatisfactory, and on auscultation the respiratory sounds are harsh and bronchitic. Not uncommonly slight touches of pleurisy are experienced in the severe and protracted cases. Dysp-

nœa may be noted, and often without any grave condition being found on physical examination to account for it. Pneumonic consolidation is rare, not occurring in more than two per cent. of cases.

Circulatory System.

Palpitation of the heart becomes developed in many. The pulse may be said to range between 70 and 120. During the first period of the disease, although the temperature may range high, the pulse is frequently found to remain low, 80 to 90. As the fever progresses and the heart becomes weakened it rapidly increases, so that about the fortieth or fiftieth day 110 or 120 beats per minute are often registered. The highest pulse rate I have noted in a non-fatal case was 132 on the seventy-eighth day of disease.

Blood and Blood Glands.

Only in rare cases are particles of pigment to be seen on examining the blood with the microscope. The red blood corpuscles, as a rule, fall from 5,000,000 per cubic millimetre to about 3,500,000. The white blood corpuscles in most cases are found to be normal in number. The spleen is always enlarged, frequently painful on pressure, and in a few cases severe pain is complained of in this region.

The Temperature.

On looking over a series of temperature charts of this fever, the first thing which strikes one is their extreme irregularity. It is also seen that in the great majority of cases this fever belongs to the continued type, the difference between the morning and evening temperature being only from one to two degrees; but in a few cases there is seen a tendency in the fever to assume a remittent or even intermittent type, the temperature being normal or slightly above normal in the morning, and rising to 104° or 105° F. in the afternoon.

Mild, uncomplicated cases show a curve touching 103° or 104° F. during the first week or ten days, and gradually sinking down to normal limits from the fifteenth to the twentieth day, when convalescence begins and recovery is uninterrupted.

But in the ordinary typical cases of this fever the course is much less satisfactory, as will be seen by the following chart (Fig. 22), which shows the long course of the fever, and the relapses which occur so frequently in this disease.

The first wave of temperature is seen in the following chart (Fig. 22) to rise to 105.4° F. and then to sink gradually down to the normal line, which is reached about the twenty-sixth day. Then follows a

week or ten days of apyrexia, followed by a second wave, the crest of which touches 105.6° F., and which constitutes a relapse lasting some

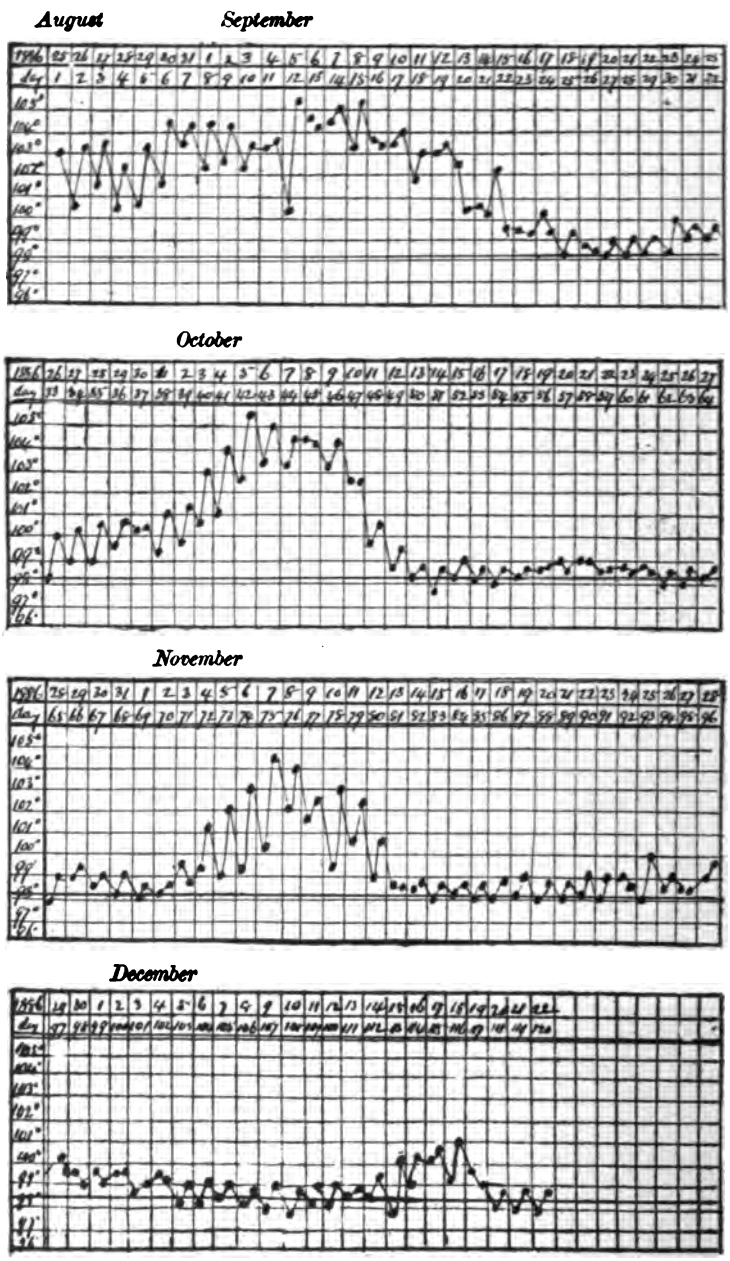

FIG. 22.

sixteen days. The temperature again remains normal, or only slightly above normal, for three weeks, when a third wave occurs, which is shorter than the foregoing, and only rises to 104.5° F.

The temperature after this second relapse is still not quite satisfactory, having a tendency to rise slightly above the normal line, and there is seen an attempt at the formation of a fourth wave between the one hundred and twelfth and one hundred and eighteenth day of disease, which, however, proves abortive, the temperature only rising to 101° F. After this the temperature remains quite normal, and the patient, although still weak and anæmic, is shortly afterwards sent back to his regiment to be employed for the first month on light duty.

That these secondary waves or relapses may persist for a very long time is shown by the next chart (Fig. 23) on which two are repre-

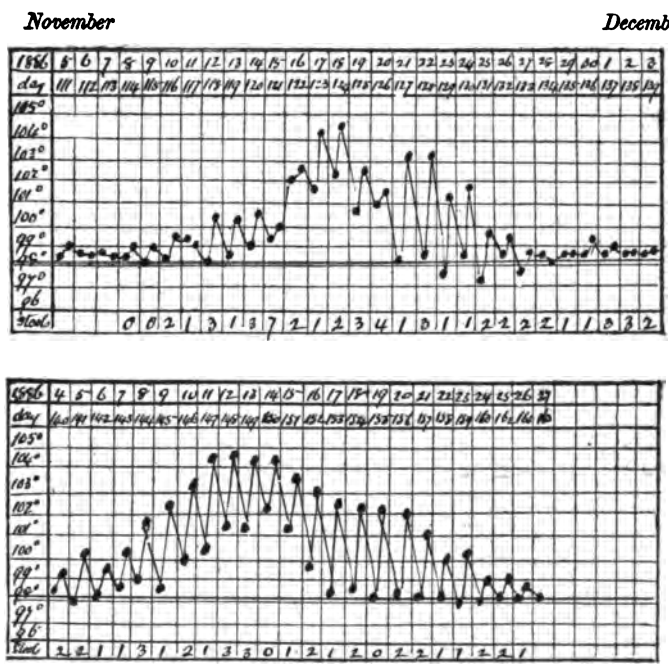

FIG. 23.

sented as occurring between the one hundred and fifteenth and one hundred and sixtieth day of the disease.

Although there is a marked tendency in the temperature curve of Malta fever to exhibit an undulatory course, such as has been represented, nevertheless few cases occur in which the waves are separated by such regular periods of apyrexia. In most cases the temperature

remains a degree or two above the normal between the different recrudescences, and in many the fever is so irregular as to partially or completely mask the wave-like character.

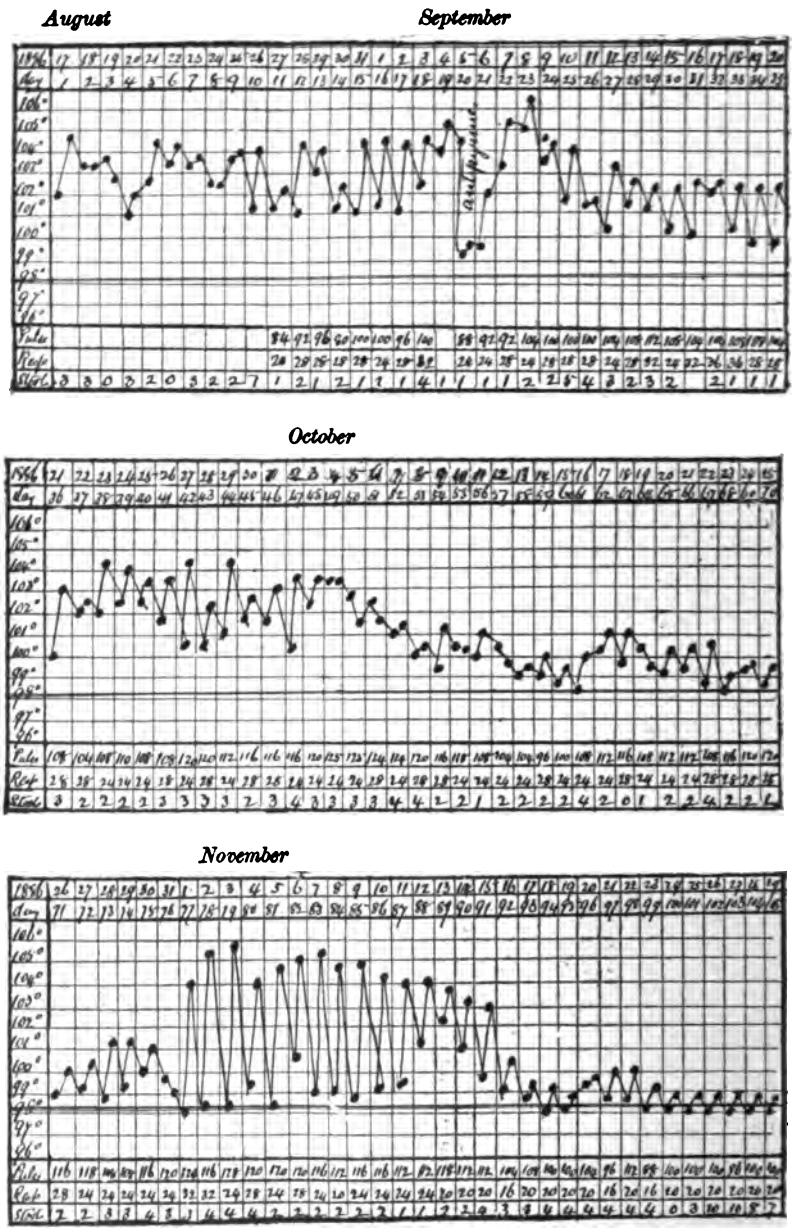

FIG. 24

Such an irregular case is presented in the preceding chart (Fig. 24), in which the temperature only fairly reaches the normal limits on the one hundredth day. On examining this chart it will be seen that the first and second waves are separated by a period, not of apyrexia, but merely of lowered temperature, and that between the second and third waves the temperature is also above the normal line except at a few points.

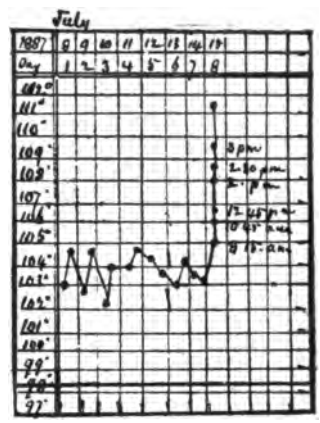

FIG. 25.

The third wave, from the seventy-seventh to the eighty-seventh day, is interesting, as being a well-marked example of the temperature assuming the intermittent type, which, as mentioned above, sometimes occurs in this fever, the temperature at 8 A.M. being normal, whereas at 2 P.M. it has risen to 105° F. and even one day to 105.8° F.

In fatal cases the temperature usually runs up rapidly shortly before death, reaching 110° F. or, as is illustrated by the accompanying chart (Fig. 25) as high as 111.5° F. This high temperature was noted by placing a thermometer in the centre of the liver ten minutes after death.

Genito-Urinary System.

One of the most painful complications in Malta fever is orchitis; but fortunately this is not of very common occurrence, and usually after a few days the inflammation and swelling of the testicle pass away without further untoward result. Albumin appears in the urine in the most severe cases, but this is a somewhat rare occurrence. Retention may occur, and must be guarded against.

Tegumentary System.

Perspiration is one of the characteristic symptoms of this fever, hence the name febris sudoralis. In about one-half of the cases it may be said to be profuse. Crops of furunculi sometimes occur towards the end of the disease, and purpuric patches may be noted in severe cases. Sudamina in greater or less number are almost invariable, but nothing corresponding to the rose-colored eruption of typhoid fever is met with. Towards the conclusion of the fever the hair frequently falls out extensively.

Nervous System.

Delirium occurs, especially at night, in about one-sixth of the cases, and sleeplessness at the beginning of the illness is the rule. I have noted partial loss of memory in some cases, and irritability of temper occurs not infrequently. Want of sensation in some parts of the cutaneous surface is sometimes met with, as also the opposite condition of hyperæsthesia. Loss of muscular power, and even paralysis of certain muscles, may occur in rare cases, and this condition may persist for several months. Headache is severe in more than a third of the cases—usually frontal, next in frequency occipital, and least commonly confined to the vertex. Pain in the lumbar region is a frequent symptom; and sciatica in one or both nerves occurs in about one-twentieth of the cases.

Joints.

Pain and swelling of joints, a very important symptom, is noted in nearly half the cases. The joints most commonly affected are the shoulders and knees, next in frequency the hips, then the elbows and wrists, and lastly the ankles. The amount of effusion, say in the knee-joint, may be very considerable, but in no case have I seen suppuration occur.

Special Senses.

In about a tenth of the cases dulness of hearing is complained of; and in very rare cases a patient is found who complains of dimness of vision.

Diagnosis.

Malta fever differs clinically from typhoid fever principally in being of longer duration, in the absence of the characteristic rose-colored eruption, in constipation being the rule instead of diarrhœa, in the frequent presence of painful articular complications, and finally, in the much smaller rate of mortality.

But it cannot be denied that many severe cases occur which so closely simulate severe cases of typhoid that for the first week or two it is impossible to be absolutely sure of their nature, except by post-mortem examination. After such cases have been under observation for several weeks, the clinical differences tend to become more manifest, and there is usually then no difficulty in separating the one from the other.

It is probable that a comparison of the behavior of the micrococcus of Malta fever and the typhoid bacillus to serum taken from

Malta fever cases may be found of practical use in diagnosis. It is in such a case as this, where two fevers difficult to distinguish from each other exist side by side, that the method of serum diagnosis may be expected to give good results. Professor Wright of Netley seems to have shown that by this method the diagnosis may be made with ease and certainty.

Prognosis.

Duration of the Fever.

Soldiers show an average stay in hospital of ninety days; but the length of the fever varies between very wide limits in different individuals. While some return to duty after twenty or thirty days, others again remain in hospital for as many weeks or more. One case which came under my observation was admitted to hospital in July, and with the exception of February and March he was in hospital suffering from this fever and its sequelæ until the end of the following year.

Rate of Mortality.

Not the least extraordinary feature of Malta fever is its low death-rate. From the result of my observations I would put it as low as two per cent., which is very different from that which obtains in typhoid fever.

Immunity from Second Attack.

Some writers state that this disease is often manifested more than once in the same individual; and in the navy this opinion is held so strongly that officers and men who have once had Malta fever are not sent back to this station until a long time has elapsed. So far from one attack granting immunity, it is believed to predispose very strongly to a second and third attack. In a fever of such indefinite duration, cases of which may last two years, there is always the danger of mistaking a relapse for a second attack. My experience leads me to the general conclusion that, as in many other infective diseases, one attack of this fever does as a rule confer immunity.

Treatment.

Prophylaxis.

Those who find it convenient to spend the hot and unhealthy season away from the Mediterranean in more temperate climates should do so. Failing this, a partial migration from the overcrowded

cities to the neighboring country may be recommended. The many who can do neither should carefully examine the sanitary state of their dwellings before the hot weather sets in. The house drains should be tested for leakage, it should be seen to that they are properly trapped, and they should be kept thoroughly flushed. The water supply should be also looked to. Everything liable to decompose in the house or surroundings should be burnt or otherwise disposed of. Care should be taken to avoid overcrowding of sleeping apartments, and that nothing prevents their being flushed with fresh air and sunshine at suitable hours. Personal health should be attended to, since overfatigue of mind or body, intemperance, exposure to chills, etc., strongly predispose to the disease.

Therapeutics.

It may be stated at the outset that there is no specific medicinal treatment known for combating this fever and that the majority of the cases are best treated by leaving out drugs as much as possible.

On account of the name remittent fever being commonly associated with the disease, most medical men at first treat it by giving large doses of quinine. As the result of many observations on the action of this drug in Malta fever, I can assert that quinine has absolutely no beneficial influence whatever, and if pushed, as is too often the case, is deleterious. There is also a great temptation, on account of the frequency of joint complications, to use salicylic acid and the salicylates, but experience soon shows that these drugs are also quite useless.

In this disease, as in many others, our therapeutic management must still remain in the unsatisfactory position of treating symptoms as they arise. High temperature is one of the most important of these, and one of the most difficult to treat. Antipyrin, given to the extent of sixty or ninety grains in two or three doses, at intervals of an hour, causes a fall of temperature of many degrees in a few hours; but the return rise is just as remarkable for its rapidity, and I have never seen any real benefit accrue from its use.

The application of cold is probably the best method of combating this symptom; but, to be of any use, this therapeutic means must be carried out thoroughly. Cold sponging and wet pack may be useful in moderate cases; but to save life when hyperpyrexia threatens to supervene, immersion of the body in the cold bath is necessary. This may require to be repeated for some days, every three or four hours, night and day, and is a method of treatment difficult to carry out thoroughly. The patient is placed at first in water at a temperature of 80° or 85° F., and this is then cooled down

some fifteen or twenty degrees by placing ice in the water. At the same time, a quantity of cold water may be dashed over the patient's head from time to time. Ten minutes is about the usual time required for each immersion, during which time a little brandy should be given. The temperature in the rectum must be taken every hour, and the bath repeated as soon as the body heat tends to rise above 103° F.

Sleeplessness is another symptom which may require to be treated at the beginning of the illness. As a rule, this soon passes off; but a full dose of antipyrin, or chloral with bromide of potassium, may sometimes be useful. Headache also usually disappears for a time shortly after the administration of antipyrin; and the same drug may be tried if the lumbar pain presses for treatment. The painful affection of the joints is best treated by local applications, such as painting with iodine or gently rubbing with one of the ordinary liniments; and for the sake of protection the joint should be enveloped in cotton wool. The orchitic complication is relieved by hot fomentations, to which belladonna or opium may be added, and by the careful support of the inflamed testicle. Constipation is best relieved by enemata, or by some simple aperient, such as castor oil.

Diet.

As there is a great tendency to gastric irritability in this disease, every care should be taken regarding the diet. During the first days of the fever, milk alone will be found best, then beef-tea or chicken-broth may be added. Raw eggs beaten up in milk are also well borne. In many cases the addition of stimulants will be found necessary. I would specially mention at this point that as this diet of milk, beef-tea, eggs, and brandy may require to be continued for several weeks, it is most essential that lemonade made from fresh lemons or lime juice be added to prevent the occurrence of scorbutic symptoms. After the acute stage of the fever has passed, the monotony of the diet should be varied as much as possible by giving part of the milk in the form of rice pudding or custard. There can be no hard-and-fast rule as to when mild solid food, such as fish or chicken, may be given—each case must be judged for itself; but the transition should be gradual, and not till the temperature has fairly come down to the normal, and remained there for a fortnight, should the patient be promoted to ordinary diet.

Change of Climate.

Finally, the question of the benefit of a change of climate may be touched upon. I do not hold, as many do, that it is as necessary to get patients out of the infective area of Malta fever as in the case of malaria. I rather look on Malta fever and typhoid as being similar in this respect, and that patients will throw off the disease and recover perfectly without leaving the island. By saying this, I do not wish in the least to disparage the benefit of change of climate which common experience proves to be so great, but to combat the exaggerated notion which prevails among many, that every effort must be made to hurry their fever cases out of the island.

On account of this mistaken idea, many invalids are sent to England while still suffering from the fever and in an extremely debilitated condition, to bear the misery of a sea voyage, and to pass the long period of convalescence exposed to the vicissitudes of an English winter, when the climatic conditions of Malta are just becoming favorable.

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